

3rd CONGRESS OF TOXICOLOGY IN DEVELOPING COUNTRIES
CAIRO, EGYPT 19 - 23 NOVEMBER, 1995.



THEME

TOGETHER FOR HUMAN AND ENVIRONMENTAL WELFARE

INTERNATIONAL SYMPOSIUM A

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Under the Auspices of

His Excellency President

MOHAMED HOSNY MUBARAK

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VENUE

Opening Ceremony: Cairo International Conference Center (CICC)

Scientific Programme : Egyptian Petroleum Research Institute (EPRI)

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ABSTRACT

DIGEST

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Preface

The *1st. Congress of Toxicology in Developing Countries* was held in 1987 at *Buenos Aires, Argentina* ; the *2nd.* was in 1991 at *New Delhi , India* . Both were successful and encouraging in stimulating exchange , progress and improvement in facing the diverse , unique or more intense problems linking toxicology with the needs of the Developing World . Cooperation , understanding and exchange of knowledge with toxicologists from the Developed Nations were the key of past success .

As a continuation on the same road , the *3rd. Congress of Toxicology in Developing Countries , Cairo , Egypt* aims at providing a platform to the toxicologists and scientists working in allied disciplines to discuss the important issues in toxicology and the latest developments among themselves and with their colleagues in developed countries.

This *issue* includes abstracts and topics presented in the Cairo Congress . At a glance , the Scientific Programme consists of **35** invited lectures , **13** oral sessions, **98** poster presentations of **12** topics , **2** symposia , and **2** workshops. Moreover, **4** roundtable discussions on subjects of global concern are included .

It's hopefully that this *Book* will be of benefit to everybody concerned with toxicological and environmental sciences .

Vice President & Secretary General
Prof.Dr. Sameeh A. Mansour
Professor of Environmental Toxicology
National Research Centre
Dokki , Cairo , Egypt.

PLENARY LECTURES

Main Topics

- * Monitoring Environmental Pollutants
- * Neurotoxicity of Toxic Chemicals
- * Biodegradation & Remediation Strategies
- * Molecular Mechanisms of Neurotoxins
- * Toxicity Interaction & Complication
- * Drug Toxicology
- * Toxicological Problems & Management
- * Immunotoxicity & Carcinogenicity
- * Biological Markers & Risk / Safety Assessment
- * Cellular Mechanisms & Regulation
- * Toxicological Data Base & Control Strategies
- * Environmental Toxicology

Monitoring Environmental Pollutants

PL 1.1

NEW STRATEGIES FOR THE EVALUATION OF THE CARCINOGENIC ACTIVITIES OF CHEMICALS.

B.A. Schwetz.

FDA/ National Centre for Toxicological Research, Office of the Director, 3900 NCTR Road, Jefferson, Arkansas 72079 U.S.A.

Carcinogenicity testing today normally includes the conduct of two- year studies in rats and mice of both sexes, following widely accepted procedures for husbandry, selection of dose levels, pathology and toxicity observations, and statistical interpretation of tumor data. These studies are usually preceded by tests for genetic toxicity and subchronic toxicity studies to select dose levels for the two- year studies. While these data are used for quantitative risk assessment, the mechanistic basis for effects is usually unknown and the series of studies is very expensive and requires five or more years to conduct. Alternate approaches are being developed that would provide more mechanistic information and would hopefully permit decisions to be made about carcinogenic potential without the need to conduct two - year studies in rats and mice of both sexes. Decisions could be based on a profile of data rather than the result of one test. Procedures for regulatory acceptance of new approaches for carcinogenicity testing must be developed.

PL 1.2

BIOSENSOR TECHNOLOGY FOR MONITORING ENVIRONMENTAL POLLUTANTS.

Mohyee E. Eldefrawi

Dept. of Pharmacology, Univ. of Maryland School of Medicine, Baltimore, MD 21201, U.S.A.

Biosensor technology is a novel approach for detection and quantitation of environmental pollutants. Biosensors are analytical devices that couple biological material (e.g. enzyme, receptor, antibody or a living cell) to a variety of transducers. We have utilized potentiometric biosensor and fiber optic evanescent fluorometric immunosensor, for detection and quantitation of organic chemical pollutants. Recombinant technology is used to clone antibody (Ab) genes in *E. coli*, that are highly selective for the toxicant of interest. Fluorescent reagents are synthesized by cross-linking fluorescein to the chemical pollutant, thereby generating a fluorescent signal upon binding to the Abs that are covalently immobilized on the quartz fiber. The bound fluorescent chemical is excited by the evanescent light wave. The presence of a pollutant (analyte) in the flow buffer competes with the fluorescent chemical for binding to mAb, thereby reducing fluorescence in a concentration dependent manner. Biosensors have been used to detect pesticides and polychlorinated biphenyls in water and soil samples. They can be regenerated for multiple use and assays are complete in minutes. The technology is cost effective and the instruments can be portable for field

use . (supported in part by US Army CRDEC contract No. DAAA015- 89- C- 000-7 and U.S. EPA agreement No. 820460020).

PL 1.3

APPLICATIONS OF BIOMARKERS FOR MONITORING AGROCHEMICALS .

Mahmoud Abbas Saleh.

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Texas Southern University, Houston, Texas 77004, U.S.A.*

This presentation is focussed on the applications and limitations of biomarkers of agrochemicals for exposure, effect susceptibility and dose. Numerous biomarkers have been developed and demonstrated in the laboratory in recent years, and now are being tested in real world setting. These methods are being increasingly applied because exposures that were once recognized only in the workplace now are known to be occurring environmentally to a much wider population. Biomarker data, therefore, have been considered as complementary to occupational or environmental exposure data in estimating hazard or risk. Now biomarker data are coming into their own as a method for interpretation, and setting of pharmacokinetic modeling. As the technique evolved, these biomarkers are beginning to be related to effect, and are progressing toward their ultimate clinical applications. Examples of biomarkers to be presented include; Markers for body burden, Enzymes biomarkers, receptors biomarkers and adducts to proteins and macromolecules.

Neurotoxicity of Toxic Chemicals

PL 2.1

ROLE OF METALLOTHIONEIN IN CADMIUM HEPATOTOXICITY

Curtis D. Klaassen.

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Cadmium is an environmental pollutant that is toxic to a number of tissues. Acute exposure to Cd produces severe liver injury, which can cause death. Chronic exposure to Cd also causes liver injury, followed by renal damage. Tolerance to both acute and chronic Cd toxicity exists. To determine the importance of metallothionein in Cd distribution, and the mechanism of tolerance to Cd lethality and hepatotoxicity, experiments have been performed in animals in which metallothionein has been induced with Zn and Cd, in newborn animals which have high concentrations of metallothionein in their livers, as well as in MT- transgenic and MT- null mice. The studies demonstrate that (1) MT does not produce a marked change in the distributions of Cd to the target organs. However, it alters the subcellular distribution of Cd, with more distributing to the cytosol bound to the small- molecular weight protein, metallothionein (2) MT plays an important role in Cd-induced liver injury by sequestering Cd in the cytosol and (3) protective effects of Zn against Cd hepatotoxicity is mediated through the induction of MT.

PL 2.2

ROLE OF NITRIC OXIDE IN HEALTH AND DISEASE IN BRAIN

Durisala Desai

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39216, U.S.A.*

Nitric Oxide is a free radical generated in a number of tissues on demand to act as second messenger molecule. Calcium when binds with calmodulin activates neuronal Nitric Oxide synthase which converts L- arginine to L- citrulline and Nitric Oxide. At physiologic levels this molecule regulates a number of functions in the brain including the synaptic plasticity. Nitric Oxide, however, when generated in excess causes neuronal dysfunction. Improper neurotransmission has been implicated in stroke, ALS, Alzheimer's disease, spinocerebellar Ataxias. Nitric Oxide has been shown to regulate a number of neurotransmitter pathways and modulation of Nitric Oxide levels leads to neuronal dysfunction and death. A review of literature as well as studies from our laboratory on human brain Nitric Oxide synthase will be presented.

PL 2.3

MANGANESE- INDUCED NEUROTOXICITY : RECENT ADVANCES IN EXPERIMENTAL RESEARCH.

Syed F. Ali, H.M. Duhart, G.W. Lipe, L. Schmued and W. Slikker, Jr.

Neurochemistry Laboratory, Division of Neurotoxicology, National Center for Toxicological Research, FDA Jefferson, AR 72079- 9502, USA.

Manganese (Mn) is an essential element, the deficiency or excess of which, is known to cause neurotoxicity in experimental animals and man. The mechanism of action of Mn-induced neurotoxicity is still unclear. We hypothesized that Mn-induced neurochemical changes are produced via oxidative stress. Several experiments were conducted to test this hypothesis by measuring the formation of reactive oxygen species (ROS), lipid peroxidation and monoamines concentration along with neurohistological evaluation in cerebral tissue. In vitro exposure to Mn increased the formation of ROS in brain synaptosomes of rats of different ages, however neonatal brain was observed to be more susceptible than adult brain. In follow-up experiments two different valence states of Mn were tested. Results revealed that in Vitro exposure to divalent Mn, (MnCl₂; 1-1000 uM) produced dose- dependent increases of ROS in striatum whereas trivalent Mn, (MnOAC; 1-1000 nM) produced similar increases at a much lower concentration. In vivo exposure to MnOAC (Mn⁺³) produced significant increases of ROS in caudate nucleus and hippocampus, whereas only the high dose of MnCl₂ (Mn⁺²) produced significant effects in hippocampus. Intracerebral injection of Mn⁺² results in a relatively restricted lesion, while the same molar concentration of Mn⁺³ produced a moderately large lesion. These and our previous data suggest that both divalent and trivalent manganese induce ROS, however, Mn⁺³ is 100- times more potent than Mn⁺². Therefore, collectively, it can be concluded that these results

support the hypothesis that the neurochemical changes induced by Mn may be mediated via ROS and oxidative stress.

Biodegradation & Remediation Strategies

PL 3.1

ALTERNATIVE TECHNOLOGIES FOR BIODEGRADATION OF HAZARDOUS CHEMICALS.

James J. Valdes

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The Chemical weapons convention requires the destruction of all chemical agents. The primary agents are organophosphorus (op) nerve agents and mustard, the latter a powerful vesicant, stored in both munitions and bulk containers. The U.S. has approximately 25,000 tons of these chemicals which must be destroyed. The initial plan to incinerate the agents has met with political and public opposition, and alternative technologies are currently being evaluated as substitutes. Enzymatic detoxification of nerve agents was demonstrated using organophosphorus acid and anhydrolases isolated from *Alteromonas*, a moderately halophilic soil bacterium. The enzyme degrades roughly 100x its weight per minute, although it varies for different op's. Mustard mineralization has been demonstrated by alkaline hydrolysis to thiodiglycol (TDG) followed by microbial biodegradation of the TDG. In both cases, the products are CO₂, H₂O, and salts. These processes are now being scaled up, and process optimization and cost analyses being performed. Systems design and applications to biodegradation of related pesticide chemicals will be discussed.

PL 3.2

BIOREMEDIATION OF AGRICULTURAL WASTES INTO USEFUL PRODUCTS.

Murray Moo-Young and Yusuf Chisti

Industrial Biotechnology Chair University of Waterloo, Waterloo, Ontario, N2L 3G1, Canada.

Agricultural wastes in the form of animal manures and crop residues are potential environmental pollutants if left untreated. Bioconversion of these waste materials as fermentation media in bioreactors offer a socio-economic opportunity of producing useful products from them while concurrently eliminating the biohazards they pose. Bioprocessing strategies have been developed for the bioconversion of manures and straws into biogas - fuel methane and / or microbial biomass (SCP) as proteinaceous animal feed ingredient for soymeal replacement / supplement. The relevant biotechnologies seem appropriate for application for various scenarios in both developed and developing countries.

PL 3.3

ECOTOXICOLOGY AND ENVIRONMENTAL MONITORING IN THE REPUBLIC OF KOREA AND UNIDO STRATEGY .

k. kim¹, D.H. Yeom¹, S.K. Lee¹, C.Y. Chang², W. Kim³, S.A. Yoo⁴ and Y.-H. Kim⁵.

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With rapid industrial development, thousands of chemicals are being used causing human and ecological concern. Pesticides are one of the important group of chemicals of concern. Two studies on pesticides in this regard will be summarized: one for ecotoxicological assessment of existing pesticides, the other for assessing a new pesticide to be introduced to south Korea. The study is on the effect of diazinon to aquatic species at the field concentrations. A run - off study was performed for registration of an insecticide to be used for potatoes. Run - off water was chemically analyzed and tested for toxicity to fish *in situ*. UNIDO provides support services in strengthening national capabilities of ecotoxicology and environmental monitoring of chemicals in developing countries. Three related projects have been completed or under provision in the republic of Korea, Pakistan and Kuwait with cooperation of UNDP and Danish government. Projects are under development for Afro-Arab region, Eastern Europe and Latin America.

Molecular Mechanisms of Neurotoxins

PL 4.1

NEUROTRANSMITTER RECEPTORS AS TARGETS FOR INSECTICIDES

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Neurotransmitter receptors are vital proteins that are responsible for regulating cellular function in nerve cells, muscles and glands. The mechanism of neurotoxicity of several toxins and toxicants is explained by their actions on these receptors. Neurotransmitter receptors belong to two major classes: *Ionotropic receptors*; (e.g. nicotinic, glutamate, GABA receptors) which are multimeric ligand- gated ion channels responsible for quick responses resulting from net ion influx into the cell, causing membrane depolarization or hyperpolarization. *Metabotropic receptors*, which are composed of a single subunit and are G- protein- linked, transduce their signals by activating or inhibiting specific second messenger systems. Nicotinoids, neonicotinoids and nitromethylene heterocyclic insecticides act as agonists of nicotinic acetylcholine receptors, while organophosphorus anticholinesterases bind directly to and activate muscarinic acetylcholine receptors. Subchronic exposure of rats to parathion produces significant down- regulation of the m1, m3 and m4 mRNAs of muscarinic receptor

subtypes in frontal cortex and striatum, but not the m1 in the hippocampus. Avermectins directly activate the GABA_A receptor's Cl⁻ channel, by binding to a unique site, while cyclodienes (e.g. α endosulfan) are potent noncompetitive inhibitors of the GABA_A receptor's Cl⁻ channel. The use of the Cytosensor microphysiometer to study insecticide toxicity on cells expressing specific receptors will be discussed (supported by U.S. Army IPA Assignment Agreement)

PL 4.2

MOLECULAR MECHANISMS OF NEUROTOXINS IN PLANTS USED FOR FOOD.

Peter S. Spencer

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(Abstract not received)

PL 4.3

INTERACTION OF PESTICIDES WITH NEUROTRANSMITTER RECEPTORS AND ASSOCIATED SECOND MESSENGER SYSTEMS.

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Three major types of membrane receptors are involved in signal transduction including: chemically gated ion channels resulting in cell membrane depolarization (excitatory nicotine and glutamate) or hyperpolarization (inhibitory GABA and glycine), linked to the guanine nucleotide binding proteins (G. proteins) that transduction mechanism depends on the formation of intracellular second messenger substances and growth factor receptors. Many vulnerable proteins involved in signal pathway can be directly affected by pesticides, these include the enzyme(s) synthesizing or metabolizing neurotransmitter, the release and uptake of neurotransmitter or its precursor, the receptors, and postsynaptic events associated with receptor activation. Upon receptor activation, signal pathways that ultimately regulate cellular processes (e.g. secretion, contraction, metabolism or growth) via second-messenger substances. Although the number of second messenger systems are very small, it involves several amplifying enzymes, G proteins, regulatory and catalytic protein subunits that might be targets for pesticides. The direct interaction of pesticides with the receptors and their associated second messenger systems will be highlighted specially cholinergic system and its events related to nicotinic receptor (chemically - gated ion channel) and muscarinic subtype receptors (G protein, second messenger substances formation, cAMP, cGMP, diacylglycerol, inositol triphosphate, and nitric oxide).

Toxicity Interaction & Complication

PL 5.1

THE INFLUENCE OF DIETARY UPTAKE ON CHEMICAL TOXICITY.

Ronald W. Hart, Angelo Turturro, Peter H. Duffy, Ritchie J. Feuers, Ming Hsiug Lu, and Julian E.A. Leakey.

National Center for Toxicological Research /FDA, Biometry and Risk Assessment, HFT-020, 3900 NCTR Road, Jefferson, AR 72079, USA.

The toxicity of numerous chemical agents can be significantly altered by the quantity and quality of dietary intake. In fact, a simple reduction in caloric intake in the presence of a nutritionally dense diet has on numerous occasions been shown to significantly alter the rate of occurrence of various spontaneous and chemically induced degenerative disease processes. Since reducing individual dietary components (such as protein or fat without reducing the overall caloric intake) is less effective in increasing longevity or suppressing neoplasia than caloric reduction by itself, it is reasonable to assume that the observed effects of reduced caloric intake, in the presence of such a diet, is the primary determinant for dietary modification of toxicity, and not any specific dietary components. Since dietary intake varies greatly between individuals and cultures, understanding these differences and how they impact upon chemical toxicity is fundamental to the proper calculation of risk. The effect of macronutrient restriction will be discussed in terms of its effect on the interface of a chemical agent with an organism, its disposition, metabolism, and interaction with macromolecules. The significance of these findings on animal testing and human epidemiological studies will be covered.

PL 5.2

THE JOINT NEUROTOXIC ACTION OF ORGANOPHOSPHOROUS INSECTICIDES.

M.B. Abou-Donia

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Chlorpyrifos is an organophosphorus insecticide which produces delayed neurotoxicity in humans and chickens following high level, acute exposures. Organophosphorus compound-induced delayed neurotoxicity (OPIDN) is characterized by delayed period of 6-14 days before onset of ataxia and paralysis in severe cases. Adult hens were given a single 100 mg/Kg oral dose of chlorpyrifos or Saffrotin, alone, or in combination. The oral LD50 for chlorpyrifos and Saffrotin in hens were determined to be 35 and 50 mg /Kg, respectively. Hens were sacrificed 24 and 96 hr following treatment and brain neurotoxicity target esterase (NTE) and plasma and brain cholinesterase activities were determined. Other hens were allowed to survive 16 days, evaluated for OPIDN and sacrificed for histopathological examination. Exposure to high levels of Saffrotin ($\geq 2 \times$ the LD50) did not significantly inhibit NTE activity compared to controls or produce signs of OPIDN. Chlorpyrifos treatment resulted in $<50\%$ inhibition of NTE and signs of mild ataxia and disturbance of gait were present

at 16 days. Combined treatment with 100 mg/ Kg oral dose of each compound produced 71% inhibition of NTE and paralysis. Spinal cord tissues showed degeneration and enlarged axons in the lateral and ventral tracts that are typical of OPIDN. Co-exposure to chlorpyrifos and Saffrotin resulted in increased inhibition of brain NTE and development of OPIDN at dose level which do not produce these effects when each compound was given alone.

PL 5.3

MECHANISMS OF INTERACTIVE HEPATOTOXICITY : HOW ONE CHEMICAL INFLUENCES THE TOXICITY OF ANOTHER.

I.Glenn Sipes

Center for Toxicology, Program in Pharmacology/Toxicology, College of Pharmacy, University of Arizona, Tucson, AZ, USA.

The hepatocyte is one of most vulnerable cells types within the body with respect to chemical exposure (dietary constituents, environmental pollutants, etc.). Thus, chemical - induced liver injury is of great concern. However, recent findings from laboratories throughout the world, suggest that other cell types within the liver play critical roles in the development and progression of chemical -induced liver injury. One cell type is the Kupffer cell, the resident macrophage of the liver. By releasing a variety of bioactive factors (reactive species of oxygen, various cytokines, proteases, etc.), the Kupffer cell influences greatly the development of liver injury. Various dietary constituents (i.e. retinal), environmental pollutants (lead, dichlorobenzenes), ethanol and disease states, influence the activity of Kupffer cells and ultimately, the development of liver injury. Understanding how the Kupffer cell is primed, activated and inhibited and what mediators it releases, is crucial to understand how these cells interact with the hepatocyte and other cell types within the liver. Various cellular and molecular approaches are being used to understand these interactions. Supported by NIEHS ES06095 and ES06694.

Drug Toxicology

PL 6.1

TREATMENT OF CHEMICALLY- INDUCED FREE RADICAL MEDIATED CELL INJURY.

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Many chemicals cause cell injury via production of free radical intermediates which via H abstraction, addition and other reactions with cell components initiate a chain of events eventually ending in cell death and the later occurring necrosis. During the past 26 years or so, our laboratory studied the model system carbon tetrachloride- liver and after learning about the steps involved in the process developed effective treatments preventing damage based on mechanistical reasons. Possibilities for prevention

formed ; blocking of $*R$ promoted lipid peroxidation. These early events perturb calcium homeostatic mechanisms to increase intracellular Ca^{++} concentration which would later activate phospholipase A2, protease and endonuclease mediated degradative processes. Accordingly, prevention of CCl_4 induced liver necrosis was found with Ca^{++} chelators ; anticalmodulins; inhibitors of proteases or phospholipases and with agents inhibiting ADP- rybosilation of proteins. The potenial general validity of these treatments to other free radical mediated deleterious process is going to be discussed.

PL 6.2

PHARMACOLOGICAL AND TOXICOLOGICAL EFFECTS OF ORGANOPHOSPHATES AND REVERSAL BY OXIMES.

S. Das Gupta

Indian Science Congress Association, 14 Dr. Biresh Guha Street, Calcutta , 700 017, India.

Organophosphorus (OP) compounds inhibit the enzyme acetylcholinesteras (AChE). This inhibition causes an increase in the acetylcholine (ACh) which causes various sympoms. Standard treatment of OP exposure consists of reactivating the phosphorylated AChE by suitable oximes and use of various cholinolytics to prevent the stimulating action of ACh. The present work will focus on the differnt aspects of medical protection against various toxic OP compounds (nerve agents) based on experimental studies carried out at the Defence R & D Establishment Gwalior for the last fifteen years. Data on some new series of mono and bispyrindinium oximes will be presented with particular reference to the efficacy of 1 alkylpyridinium oximes which were found to be more effective in Sarin intoxication as evidenced by cholinesterase reactivation in blood and cerebral cortex along withr significant reversal of neuromuscular bolckade leading to a high protection index. Prophylactic therapy in the form of pretreatment with reversible AChE inhibitors viz. Physostigmine against Sarin aersols in rodents together with a detailed study on the dynamic pulmonary mechanics along with biochemical parameters will be presented

PL 6.3

CARDIOVASCULAR SYSTEM AS A POTENTIAL TARGET FOR TOXIC INJURY: PESTICIDES, ALCOHOL, ORGANIC SOLVENTS, HEAVY METALS AND DRUGS.

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Cardiovascular toxicology is defined as the acquisition of information of the toxic effects of chemicals that are characterized by their selectivity to the cardiovascular system. The cardiovascular system is unique in its metabolic, electrophysiologic and cardiodynamic features. Although most of toxicologic studies of organophosphate, chlorinated hydrocarbon and carbamate insecticides, solvents and heavy metals have

focused on their neuro-, hepato-, and nephrotoxicity, most of these studies failed to address cardiovascular effects of these toxic materials. Because the heart is playing a crucial role in other organs viability and animal survival, it is essential to assess for cardiovascular toxicity of chemical in all assessment studies. For example, myocardial depression, low cardiac output, vasodilation and hypotension induced by unwanted chemical exposure results in compromising blood supply and oxygen delivery to the heart as well as other organs. Oxygen deprivation disrupts ATP synthesis and activates massive ATP utilization. ATP depletion impairs ionic pumps and perturb ionic homeostasis and cell volume and disturb cellular membranes integrity. These events entail activation of proteolytic enzymes and phospholipases, neutrophils and platelets, free radicals formation and ultimately lead to tissue necrosis and degeneration. Therefore, it is naive to focus only on the end point of histological changes associated with chemical poisoning and neglect the organ's functional and metabolic aspects of toxicity. In this presentation, I will discuss methods of assessing chemical induced cardiovascular toxicity and possible mechanisms of protection and possibly repair.

Toxicological Problems & Management

PL 7.1

CHEMISTRY AND TOXICOLOGY OF NERVE GAS INCIDENTS IN JAPAN IN 1994 AND 1995 .

Anthony T. Tu.

Department of Biochemistry and Molecular Biology, Colorado State University, Fort Collins, Colorado 80523, USA.

On June 27, 1994, sarin was released by the Aum Shinrikyo religious sect, resulting in 7 deaths and 600 poisoning cases. On March 20, 1995, another sarin attack took place in several subway trains and 7 people were killed and about 6 thousand people were injured by the poisoning. Sarin was produced by the Aum Shinrikyo in Kamikuishiki, Yamanashi, Japan. Sarin for the two occasions was produced at different times, and the composition of the products was slightly different. The sarin used in the Tokyo subways contained diisopropylmethylphosphonate, a byproduct of sarin formation. By raiding Aum Shinrikyo's compounds no sarin was found, although many precursors were found. The sarin was destroyed in order to eliminate criminal evidence. The National Research Institute of Police Science, however, detected two sarin degradation products from the soil near a perfab building believed to be used for the sarin manufacture. The two degradation products found were monoisopropylmethyl phosphonate and methyl phosphonic acid.

PL 7.2

TOXICOLOGY IN PROBLEM DETECTION AND AS PROBLEM SOLVING FOR TROPICAL DISEASES. THE LATIN AMERICAN EXAMPLE OF CHAGA'S DISEASE.

J.A. Castro

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Chagas' disease (American trypanosomiasis) is in Latin America a health-social and economic problem and involves more than 20 million people as already sick. Other 40 million live in areas where this disease is endemic. There are several aspects of the disease which are linked to toxicological matters. One is the toxicology of insecticides used to control the vector insect. Other is related to trypanosomocides used to prevent infection via blood transfusion (e.g. Gentian Violet) or to those employed to treat the acute phase of the disease e.g. Nifurtimox and Benznidazole. After reviewing the past contributions of toxicology to detect these problems, the recent results obtained by others and by our laboratory to attempt solving them would be presented. New insecticide less toxic formulation, are being used in Latin America national campaigns (e.g. pyrethroids) against vector, new trypanosomocides are being developed for blood banking and for disease in humans. The relevance of the contributions for Tropical Diseases of toxicology would be discussed.

PL 7.3

PESTICIDES : ADVERSE EFFECTS, REGULATIONS AND MANAGEMENT IN EGYPT.

Nabil A. Mansour

Professor of Pesticide Chemistry and Toxicology, Faculty of Agriculture, University of Alexandria, Egypt.

The wise use of pesticides to protect crops before and after harvest, during storage, in preventive medicine and in animal husbandry can lead to great improvements in food and in feed supply and quality. The last 20 years have seen a remarkable improvement in the development and adopting of procedures and approaches for defining the environmental impact of pesticides. Much has been learned in Egypt from incidents where adverse effects have occurred. There have been important advances in achieving a better definition of the aims of environmental conservation. Unwanted effects from using pesticides may be seen as falling into five main categories: carelessness or accidents; wild life poisoning; pesticide residues; pest resistance; and the environmental modification. Boundaries between adverse pesticidal effects and the inevitable consequences of the whole farming process become increasingly difficult to define as one moves deeper into this field. There can be few aspects of pesticide research where it is more important to define objectives than in the case of environmental studies. Circumstances of pesticide use are tremendously varied, the aims of conservation differ enormously between countries and so do the aims of agriculture or public health. The ultimate goal is to avoid unacceptable effects on valued environmental components.

The unacceptable effects are varying from country to country. They vary according to those who have to accept them. In fact, research should be concentrated towards looking at potential effects on all classes of non-target species. Such research consists essentially of : developing data; using it to adapt practices to minimize ill effects; and making value judgments between benefits and foreseen ill effects. It is the role primarily of the regional scientists with the local regulatory authorities for interpretation and adaptation of use recommendations. From environmental distribution to the genetic disease, it should be recognized for most pesticides, that the toxicologic paradigm, is a dose - effect relationship. In this situation we have to deal with both acute and chronic toxicity, and in some cases with the phenomena of the delayed polyneuropathy for certain compounds, like organophosphates induced delayed polyneuropathy (OPIDP). moreover, our concern was directed to the effect of pesticides on the immune system, and the adverse clinical health effects. Integrated pest management (IPM) has served as a useful biological, economical, and political paradigm for the last 2 decads. This is seen obviously in some countries and is still under implementation in others. The next logical paradigm that will carry us into the twenty - first century is to consider the production of the critical economic crops by country. Emphasis has to be devoted towards the research supporting the production of these crops, as a highly complex and dynamic system. Among those crops were priority varies by the nation corn, rice, cotton, wheat, oil seeds, leguminous or sugar cane. Researchers and managers can no longer afford to take a narrow focus. The control of a single pest species involves much more than the selection and application of a pesticide. Financial, environmental, and social costs must be considered. The multiplicity of complex factors that make up the crop production systme should not hinder researchers from addressing the problem. In fact, much of he groundwork to examine the crop production system systematically in its entire biological, physical, mechanical, economical, political, and social construct should be established through the application of systems science to pest control. It is important to founmulate the long term strategy in pest control with special emphasis on : pesticide managemnet, industrial policy and health hazards.

Immunotoxicity & Carcinogenicity

PL 8.1

TOXICOLOGICAL AND REGULATORY ASPECTS OF CARCINOGENIC MYCOTOXINS (AFLATOXINS , OCHRATOXINS, FUMONISINS).

Christian Schlatter

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Carcinogenicity is a key element in the evaluation of potentially toxic chemicals in food, because carcinogenic properties may become effective even at trace levels if they are induced by genotoxic mechanism. The elucidation of mechanisms of action is therefore not only of academic but also of practical interest. A second important step is the quantitative interpretation of experimental results in regard to the human health situation. The elaborate modern analytical techniques allow to make fair estimates of specific and average exposure situation. The extrapolation step from high to low dose levels and animals to humans is , however, still hampered by many unkown factors. As

an extremely cautious default approach a linear dose-effect extrapolation is in common use for genotoxic chemicals to set limits in food. Whereas aflatoxin is a well investigated and classical genotoxic carcinogen, this seems not to be true for ochratoxin A , although there are reports on DNA adduct formation in mice by using the 32p-postlabelling techniques. In contrast we were not able to demonstrate a direct interaction of radioactive ochratoxin with rat DNA. Ochratoxin was also negative in most mutagenicity test again indicating a lack of genotoxicity. Careful investigation of the mechanism of action of fumonisins revealed interference with the sphingomyelin metabolism which in turn has an effect of protein kinase C, a crucial enzyme in the process of cell proliferation. Fumonisin therefore are not regarded as genotoxic carcinogens but as promoters of carcinogenicity if they are present at high concentrations

PL 8.2

IMMUNOMODULATION AND CANCER

Prasanta Kumar Ray

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It is now well established that many environmental toxicants cause immunosuppression. It has been observed that persistent immunosuppressive status help in the development of malignancy. It has also been observed that after the establishment of malignancy, the cancer host develop anergy. It has, therefore, been thought logical to stimulate the host immune system using non-specific immunostimulators, so that the host could mount an immune attack against tumours. There were also some attempts as to how the tumour can be made more immunogenic. Removal of the immunosuppressors from the blood of a tumour host was yet another approach to immunomodulate the host immune response. Recent efforts are concentrated on the immunoregulators using inducers of cytokines. Also, stimulating host lymphocytes *in vitro* using cytokines and inoculating the same to the tumour bearing host is yet another approach used in experimental form of immunotherapy. Introduction of immunomodulatory gene(s) into host specific dividing cells can also be a good approach to immunostimulate the host so that the tumor bearers can mount successful immune attack to destroy the cancer cell. All these will be discussed.

PL 8.3

ROLE OF MOLECULAR BIOLOGY TECHNIQUES IN TUMOR ANALYSIS

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Elucidation of early events in tumorigenesis is a challenging issue for both oncologists and cell-biologists. Recently introduced molecular biology techniques have thrown light on some of these aspects. Analysis of integrity of cellular oncogenes, tumor suppressor and associated genes, signal transduction have led to the discovery of the involvement of several genes in the initial and late events of carcinogenesis. We utilised PCR, FISH, southern analysis to understand the status of genes such as Ras, Rb-1,

bcl-1, bcl-2, IGH, IGJ, TCR-B in a few Indian hematological malignancies. These studies have shown a good correlation between exposure to chemicals with mutation and type of malignancies which in turn were found to also be related to the prognosis of the diseases.

Biological Markers & Risk / Safety Assessment

PL 9.1

THE SAFETY / RISK ASSESSMENT OF TOXIC CHEMICALS

Frank C. Lu.

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There are two major approaches to the safety/risk assessment of chemicals. For most chemicals, there is a threshold dose below which a chemical will not exert any adverse effect. For these chemicals, the generally adopted procedure is to assess their ADIs (acceptable daily intakes). This is done by ascertaining the relevance and completeness of the database, determining the critical effect (the most sensitive yet relevant indicator of adverse effect), establishing the NOAEL and applying a suitable safety factor to arrive at the ADI. The importance of selecting a relevant critical effect is illustrated by the assessment of bromomethane. This chemical is used as a fumigant of food. After processing, storage and aeration of the fumigated food, the bromomethane is broken down into inorganic bromide. WHO assessed this fumigant and established an ADI of 1.0 mg bromide/Kg bw. U.S. EPA (1992) used the data reported by Danse et al. in which the rats were given bromomethane (not the fumigated food) by gavage. The keratosis of the mucosa in the forestomach of the rats were used as the critical effects and a factor of 1000 was applied to arrive at an RfD (i.e., ADI) of 0.0014 mg/Kg. The EPA assessment may be faulted for using an irrelevant study (bromomethane is used to fumigate the food, not for direct ingestion), and on the use of keratosis of the forestomach of rats, which is absent in humans, as the endpoint. Mathematical modeling is used for the assessment of genotoxic carcinogens. Examples with this procedure will be presented at the congress, comparing the merits of the "Maximum Likelihood Estimates" with the "Most Conservative Estimates" and the need for indicating the uncertainty of the estimates. A knowledge of the magnitude of the uncertainty may allow a more rational management of risks.

PL 9.2

BIOLOGICAL MARKERS FOR TOXICITY ASSESSMENT AND HAZARD PREDICTION OF ENVIRONMENTAL CHEMICALS.

Mervyn Richardson

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The proliferation of chemical substances having the potential to pollute any environmental media (air, land, water), or humans via occupational exposure, is considerable. Chemical abstracts now lists >12 million substances and > 100,000 have been notified for industrial use within the European Union. Whilst chemical analytical

techniques exist for the measurement of some of these chemicals, many of the methods involve costly techniques of considerable sophistication- quantification may be even more involved. Whilst hazard data, eg, reliable quality toxicology and ecotoxicology data has been ascertained by tests using mammals, fish and other organisms there are often too few data on many chemicals. Data on many natural products, the toxicity of which in some cases can be more acute than any industrial chemical, metabolites found in wastewaters, byproducts of combustion either from natural (volcanos) or manmade (warfare) events are poorly documented for individual compounds or mixtures. In less developed countries where sophisticated techniques may not be available or supplies of reagents, compressed gases or even electricity cannot be guaranteed, generic techniques have a great deal to offer. An emission of a chemical will cause adverse effects to organisms and hence there is an enormous advantage in measuring such effects on biological systems. One such technique is the reduction of light output in the presence of a toxicant to the marine bacteria *Vibrio fischerii* (formerly known as photobacterium phosphoreum NRRL B- 11177). A dark variant M-169 can also be used to obtain mutagenicity data, a chronic test whose results compare well with *Ceriodaphnia dubia*, has also been developed. These techniques will be discussed. The development of the principles of Environmental Toxicology Assessment will be reviewed together with the concept of 'toxic insult' as a pragmatic tool in environmental risk assessment.

PL 9.3

PERSPECTIVES ON THE USE OF DAPHNIDS IN AQUATIC TOXICOLOGY OF PESTICIDES.

Sameeh A. Mansour

Environmental Toxicology Research Unit, Pesticide Chemistry Department, National Research Centre, Dokki, Cairo, Egypt.

In the field of toxicant bioassay, daphnids (cladocerans) have won great attention as an extremely desirable test bioindicator model due to several practical advantages. This lecture reviews a considerable number of work on daphnids, and outlines research results of special concern to the importance of using such invertebrate organisms in aquatic toxicology of pesticides. Specifically, the following topics are presented and discussed : 1) effect of intoxication criteria on *Daphnia* toxicity bioassay; 2) toxicity of insecticide mixtures to *Daphnia* ; 3) the use of *Daphnia* for quantitative bioassay of pesticide residues and persistence; 4) the use of *Daphnia* heart beat as a criterion for qualitative bioassay of pesticides; and 5) a proposed classification for evaluating toxic danger of pesticides to freshwater organisms. Subsequently, utilization of daphnids in the prediction and monitoring of aquatic pollutants, such as pesticides, is strongly encouraged.

Cellular Mechanisms & Regulation

PL 10.1

INVOLVEMENT OF SEMICONDUCTOR METALS IN GENE REGULATION OF THE STRESS PROTEIN RESPONSE.

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The III-V semiconductors gallium arsenide (GaAs) and indium arsenide (InAs) have shown to dissociate *in vivo* to release the Ga, In and As moieties. All 3 elements have been shown to alter cellular gene expression following *in vivo* and *in vitro* exposures , but the patterns of altered gene expression vary depending upon species , dose , duration of exposure, *in vivo* or *in vitro* route of exposure and gender. In general , As induces the major stress protein families including the 32 KD, 60 KD, 70 KD and 90 KD classes. Depending upon a number of the above factors , In usually suppresses the stress protein response while Ga may induce or inhibit the response depending upon exposure circumstances. *In vitro* exposure of male and female hamster and human kidney epithelial cells to these elements showed marked gender differences for both species. Induction of the 32 KD stress protein (heme oxygenase) was generally the most highly conserved response for all 3 elements suggesting that oxidative stress is probably a major underlying cause of cell injury from these agents. The general suppressive effects of In on protein synthesis may greatly compromise the stress protein response with concomitant shifts in the expected dose- response curve for the other elements. This effect should be considered in risk assessments for target organ toxicities associated with chronic exposures to these compounds.

PL 10.2

THE METABOLIC ACTIVATION OF CHEMICALS RESULTING IN TOXIC AND CANCERIGENIC PRODUCTS.

A. Benakis

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It has been reported that the majority of cancer deaths are caused by chemicals. It is evident that human beings are exposed via air, water, food and medical treatment to a great number of chemical substances such as drugs, pesticides, food additives, cosmetics, alcohol, tobacco, etc. Most of these substances are transformed into large number of new molecular species: metabolites. Depending on their chemical structures, these metabolites may have effects that are quite different from those of the parent compound. With the exception of a few direct- acting agents, the chemical carcinogens usually require the so- called " metabolic activation" in order to exert their cancer - inducing properties. The following sequence can be given: 1) all chemical carcinogens that are not themselves chemically reactive must be converted metabolically into a chemically reactive form (called "ultimate carcinogen"), 2) the activated metabolite is an

electrophilic agent and 3) this activated metabolite reacts with nucleophilic groups in cellular macromolecules (DNA and possibly RNA, proteins) to "initiate" the process of carcinogenesis. The active metabolites bind covalently to macromolecules in organelles, involving proteins, nucleic acids and lipids. If the covalent binding to nucleic acids takes place, then cancer is initiated. The parent compounds are harmless but after oxidation many of them become potent carcinogens. The activation system involves a monooxygenase system that utilizes molecular oxygen, NADPH and cytochrome P-450. Cytochrome P-450 is a well known enzyme which detoxifies and activates a wide variety of exogenous as well as endogenous compounds. Recent studies have established that there are multiple forms of cytochrome P-450 in liver microsomes, which are major organelles that metabolize drugs and toxicants. It is therefore evident that any factor affecting the enzymes involved in the metabolism of chemical carcinogens should be investigated in order to elucidate the mechanisms of action. It should be borne in mind that these factors can be endogenous such as modification of hormone equilibrium or can be exogenous compounds that are not cancerogenic in themselves but are known to be potent inducers or inhibitors of liver enzymatic systems. Furthermore, other factors such as the state of health, nutritional habits etc. must be considered. It is well known, for example, that our food contains chemical carcinogens. These are not food additives, but compounds that are naturally present in the food we eat or are produced by the way we prepare it. Among these are the naturally occurring heterocyclic compounds such as N-Nitroso compounds, aflatoxins, ascaridole, etc. The problem is more complex than was initially believed and it is hoped that a better understanding of the mechanisms involved will lead to a way of reducing the incidence of cancer as well as improving the treatment.

PL 10.3

PROBLEMS ASSOCIATED WITH MINERAL FIBERS.

Qamar Rahman

Industrial Toxicology Research Centre , Lucknow 226001 , India.

Asbestos fiber, due to its tensile strength, heat resistance, etc., is commercially exploited throughout the world. However, exposure to asbestos is associated with the development of pulmonary fibrosis (asbestosis), bronchogenic carcinoma, and malignant mesothelioma. Cell proliferation and inflammation are common features in the pathogenesis of both fibrotic and malignant regions. It has been estimated that deaths due to prolonged asbestos exposure are between 6000 to 8000 per year out of which 200 die of mesothelioma alone. Work from our laboratory and from other researchers suggests that asbestos interacts with target cells of disease through multiple mechanisms involving active oxygen species and elaboration of growth factors. In the present talk some of the aspects of asbestos-induced disorders with the highlights of current leads in the mechanisms will be discussed. The risk of asbestos-induced diseases in developing countries like India, where asbestos is being used indiscriminately along with predisposing conditions existing in Indian mines and factories, will also be discussed.

Toxicological Data Base & Control Strategies

PL 11.1

TOXICOLOGY INFORMATION RESOURCES.

Philip Wexler

National Library of Medicine , 8600 Rockville , Pike / Bethesda, Maryland 20894, USA.

A broad array of toxicological and environmental health information resources, particularly computerized, are available throughout the world. This lecture will focus on some of the major databses made available by the National Library of Medicine's (NLM) Toxicology and Environmental Heath Information Program, including the TOXNET system. Among the online files to be discussed are the Hazardous Substances Data Bank (HSDB), a databank of broad scope covering many areas related to human, animal, and Environmental Toxicology; the U.S. Environmental Protection Agency's (EPA) IRIS (Integrated Risk Information System), containing data to support carcinogenic and non- carcinogenic health risk assessments; the TRI (Toxic Chemical Release Inventory) series, another EPA sponsored project listing estimated amounts of toxic chemicals released to the environment or transferred to waste sites, as well as source reduction and recycling activities; and the extensive TOXLINE file of bibliographic information. A brief look at other relevant files within and outside NLM will also be provided, as will details on international access via telecommunications, INTERNET, and BITNIS, particularly for developing countries. Some time will also be devoted to non- computerized sources of information such as books, journals, etc.

PL 11.2

TRENDS IN THE PATTERN OF ACUTE POISONING IN ALEXANDRIA POISON CENTRE (APC).

L.A. Abd El-Megid

Forensic Medicine and Toxicology , Alexandria Poison Centre, Faculty of Medicine , Alexandria University, Alexandria , Egypt.

Alexandria Poison Centre (APC) was the first poison centre to be established in Egypt. It consists of both information and treatment units. It serves Alexandria Governorate and the surroundings. During the year 1994 , the total number of patients admitted to the APC totalled 5913, with a female sex ratio of 1.3 : 1. More than half of the patients were in the age group 15-35 years (52.3%), followed by those less than 5 years (19.4%). Just less than a quarter of patients (24.7 %) suffered food poisoning. Poisoning by household agents constituted 18.2% , followed by drug poisoning and poisoning by pesticides (16.4% and 15.5 % , respectively). Alcoholic intoxication

accounted for 8.7% while overdose by addicting drugs and substances constituted 3.1%.

PL 11.3

ORGANIZING TOXICOLOGICAL CONTROL LABORATORIES IN DEVELOPING COUNTRIES.

B.Heyndrickx

Central Laboratory Civil Hospital 9000 Ghent,Belgium

Since more than twenty years we are involved in setting up toxicological laboratories in the environmental and human care hospitals. The biggest difficulties are : constant power supplies, clean water and maintenance of equipment . It is practically impossible to run a gas- chromatograph, mass- spectrometer, etc. Therefore we were setting up a transportable toxicological unit, about 2m³ size (\pm 250 Kg) which fulfills the main needs . We use the classical standard chemical methods of wet analysis which don't need power supplies, etc. Of course they don't have the sensitivity of GC or MS, but they are reliable at any time and circumstances, sufficient to perform the screening. We checked in the field the results obtained in local hospitals and tropical areas. The samples analyzed again at home , using the most sophisticated equipment, were confirmed. In some cases the simple methods are much influenced by degraded products or metabolites. by which the original compound is too difficult to reconstruct, GC, MS, etc, are of course a supplementary confirmation. In many cases the microscope helps us in microdetermination techniques. The complete description is given for the transportable toxicological and environmental laboratory.

Environmental Toxicology

PL 12

TRANSFORMATION OF ATMOSPHERE AND BIOSPHERE BY AGROCHEMICALS.

Ahmed A. Abdel-Gawaad

Ecotoxicology Department , Faculty of Agriculture, Zagazig University , Moshtohor , Egypt.

(Abstract is included with OS 13)

PL 13

COMBINED LONG-TERM EXPOSURE TO LEAD , MERCURY AND TNT IN EGYPT.

Mahmoud M.Amr, A.M. Emara,A.H.Safwat,M.M. El-Batanouni and S.El-Dessoukey.

Occupational Disease Department , Faculty of Medicine , Cairo University and National Research Centre, Dokki ,Cairo , Egypt.

(Abstract is included with ES- 1)

ROUND TABLE DISCUSSIONS

(Abstracts Not Requested)

Main Topics & Speakers

- * R1: Assessment of Neurological Behavioural Disabilities in Children's Early Life Due to Exposure to Environmental Pollutants.**

Peter S.Spencer (USA) , D.Desaiah (USA) , R.Shukla (USA).

- * R2: Food Contamination Problems and the Need to Establishing Safety Measurements for "Multi-Contamination".**

Mohyee E. Eldefrawi (USA) , CH . Schlatter (Switzerland), Bruce Fowler (USA) , I.Glenn Sipes (USA).

- * R3: Global Strategies for Environmental Remediation.**

James Valdes (USA) , P.K.Ray (India) , M. Richardson (UK) , Sayed A. Masha'al (Egypt).

- *R4: Regulatory Toxicology Requirements and International Trade Activation :Challenges & Needs.**

Amira T.Eldefrawi (USA) , B. A. Schwetz (USA), Ronald W. Hart (USA), R. Shukla (USA).

ORAL PRESENTATIONS

Main Topics

- * Biochemical Toxicology
- * Bioremediation
- * Developmental & Reproductive Toxicology
- * Drug Toxicology
- * Environmental Toxicology
- * Genotoxicity & Carcinogenicity
- * Metal Toxicology
- * Miscellaneous
- * Monitoring Environmental Pollutants
- * Natural Toxins
- * Pesticide Toxicology
- * Preventive & Regulatory Toxicology
- * Trends to Safer Alternatives

Biochemical Toxicology

OS 1.1

IN VIVO NEUROLOGICAL AND BIOCHEMICAL EFFECTS OF KHAT (CATHA EDULIS) EXTRACTS IN MICE

Abdel khalek H.El-Sebae¹, Abdel Rahman A. M. Thabet² and Abdel Mohsen A. Komeil¹

¹*Dept. of Pesticides Chem. & Toxic. , Alexandria Univ., Alexandria, Egypt.*

²*Faculty of Agric., Sanaa Univ., Yemen Republic.*

Chewing khat leaves as a stimulant is common in certain Asian and African countries. Ethanol and water khat leaves extracts were orally administered to male and female mice (6 - 8 weeks old and weighing 28 - 30 g) in three replicates. *In Vivo* effect on AChE and MAO activity in brain and heart, and on ATPase in liver were assayed after 2, 4, 6, 8 and 10 hrs of treatment. Three levels of khat equivalent to 2.5, 5, and 10 g of fresh khat leaves / kg body weight were tested. The results indicated that males were more affected than females; and that ethanol extract was more effective as an inhibitor than water extract. At the higher khat level, maximum inhibition of MAO by 74 and 72% was recorded in male brain and heart respectively after 4 hrs. Similarly, AChE was inhibited by 67 and 64 % in male brain and heart respectively after 6 hrs. ATPase was inhibited only by 37 and 24 % in both male and female liver respectively after 6 - 8 hrs.

OS 1.2

TOXICITY OF AZINPHOS- METHYL AND ITS MAJOR METABOLITE BENZAZIMIDE IN MICE

I.M.I.Fakhr., S.M.A.D. Zayed, and Nehal A.Hamdy .

Dept. of Appl.Organic Chem.,National Research Centre, Dokki Cairo, Egypt.

Azinphos- methyl and its hydrolysis product, benzazimide were given to mice to assess acute and chronic toxicity, and to investigate possible adverse long term effects. The oral LD50 of azinphos- methyl for mice was determined to be 12.1 mg/ Kg. No fatalities occurred when mice received 100 ppm benzazimide for one day. The inhibitory action of azinphos- methyl on plasma cholinesterase activity, affected by long term feeding, did not exceed 40% after two weeks when a dose level of 12 ppm was used . On the other hand, benzazimide had no obvious effect on plasma cholinesterase of mice under similar conditions . Dietary levels of 2,4,8, and 12 ppm azinphos- methyl caused a statistically significant decrease in the amount of WBC during the first two weeks , which was dose independent . The count of the WBC increased gradually and reached the normal value within 60 days. A dose level of 48 ppm benzazimide caused a statistically significant increase in the number of WBC after two weeks. Dietary concentration of 2 ppm azinphos- methyl or 48 ppm benzazimide caused a significant increase in the SGOT indicating hepatic injury. The livers of the benzazimide treated mice were significantly heavier than those of the azinphos- methyl treated group.

OS 1.3

THE RESULTS OF SCINTIGRAPHIC AND ENZYMATIC EXAMINATION IN ACUTE CARBOFURAN IN ACUTE CARBOFURAN POISONING

M.Obara , D. Pach and L. Winnik

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An acute cholinesterase inhibitors (ChEI) result in multisystemic disorders. Common opinion that poisoning with these compounds relatively seldom damage the liver is a falsehood. The aim of the study was to evaluate the morphological and functional liver state of 12 patients treated because of acute carbofuran poisoning . The trial of establishing if the pathological changes are dependent on the degree of poisoning and on blood carbofuran concentration was also undertaken. All patients underwent scintigraphic, hepatographic and ultrasonographic examinations. The AChE, SChE, ALT, AST, GGT activities, prothrombin level, bilirubin concentration in blood were measured. Carbofuran concentration in blood was established. Results of the biochemical tests did not reveal the definite features of liver damage. In the ultrasonographic examination cholelithiasis was not found in any patient. A differently intensified changes in scintigraphic picture of the liver were found in all patients. Hepatographic picture of liver revealed the liver function lesion from 10- 35%. Of the 8 patients who underwent control scintigraphic, 5 of them were found to have the decrease and 1 person to have the increase of liver changes. The control hepatography reveals decrease of the liver damage degree in 7 patients. In the 11 of the 12 persons who showed different scintigraphic changes, the medium and severe degree of poisoning was stated on admission to the clinic. No correlation between the blood carbofuran concentration with the intensity of changes showed by scintigraphic and hepatographic examinations was noted. The liver scintigraphy , hepatography and ultrasonography combined with biochemical analysis allows to assessment of liver condition in acute carbofuran poisoning..

OS 1.4

THE EFFECT OF PESTICIDES ON THE GLUTATHIONE S- TRANSFERASE OF AQUATIC SNAIL SPECIES.

Y.S.Naik, L. Chirombe and J.A. Hasler

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Freshwater bodies in Africa face a threat from environmental chemical pollutants. Exposure of marine organisms to chemical pollutants has been shown to affect their xenobiotic metabolising enzymes. In this study laboratory reared snails (*Lymnaea natalensis*) were exposed to pesticides on a daily basis for three days. On the fourth day they were sacrificed and enzyme activity was measured using 1, cholro 2-4, dinitrobenzene as substrate. Our data indicate that the pesticides deltaprim, endosulfan, malathion and pirimphos did not alter the enzymatic activity significantly at the doses used. However, glyphosate reduced (50%), and 2,4,di- hydroxy phenoxvacetic acid increased (30%) the GST activity. The herbicide glyphosate was found to inhibit enzyme activity in four other snail species. Detailed studies using other freshwater snail species would provide information on the fate of chemical pollutants in aquatic systems.

OS 1.5

MALATHION ADMINISTRATION AND ITS EFFECT ON SOME LIVER AND KIDNEY FUNCTIONS

El- Sayed A. M. Abd Alla ¹, N.S. Ahmed ², M.N.A. Hassan and A.S.M. Fouzy²

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In this study, the highest level of malathion found in milk (2.17 ppm) and its sublethal (LD10) and lethal (LD20) doses were orally dosed to *Albino* rat and its effect on some liver and kidney functions were studied. The obtained results indicate that malathion administration has its effect on liver efficiency particularly at the high doses (LD10 and LD20) with early signs of cholestatic liver damage. Concerning the effect of malathion on plasma urea and creatinine the high doses caused some failure in kidney functions which could be considered as acute renal failure.

OS 1.6

EFFECT OF DIMETHYLSULFOXIDE ON PARAQUAT INDUCED LUNG FIBROSIS

Javade Iraj

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Paraquat (1,1- dimethy- 4- 4- bipyridylium chloride), is a broad spectrum herbicide causes lung damage in human. The specific toxicity of paraquat for lung tissue can be explained by selective accumulation in clara cells and in alveolar type I and type II epithelial cells. In this study we tested effect of dimethylsulfoxide (DMSO) in two concentrations on the development of paraquat induced pulmonary fibrosis. Male rats were divided into four comparable groups and killed by decapitation and bled after 7 days. Lung weight, lung protein, OH proline and DNA was elevated significantly 85, 125, 99 and 85% respectively in paraquat group compare with control, but these factors in animals which treated with DMSO₁, was elevated only 17, 21, 42 and 25% compare to control and with DMSO₂ were 11, 29, 31 and 28% compare to control. In conclusion it appears that DMSO prevented lung collagen accumulation when compared with, paraquat alone. These data also indicate that DMSO treatment inhibit paraquat induced lung fibrosis.

OS 1.7

TOXICOLOGICAL STUDY OF n - HEXANE IN RATS.

N.A. Abdel Maksoud¹, Azza M. Agha², H. Khalil³, H. Gamal El Din⁴.

¹Industrial Medicine and Occupational Diseases Dept., ³Pathology Dept. & ⁴Physiology Dept., Faculty of medicine & ²Pharmacology Dept., Faculty of Pharmacy, Cairo University, Cairo, Egypt.

Occupational toxicity has been reported for n-hexane among the vinyl sandal and leather workers. This study was performed on albino rats. n-Hexane was given by i. p. injection at doses of 75, 150 & 300 mg / kg twice a week for 8 weeks in groups I, II & III respectively. A control group receiving the solvent (1% Tween 80) only was performed. Results of this study revealed that the brains of the exposed rats did not show any significant change in O₂ uptake however, they showed marked histopathological changes. There was significant decrease in O₂ uptake by the livers of groups I, II and III (70, 35, & 4 mg / 100 g wet weight respectively) as compared to control (119 mg/ 100g wet weight) : in conjunction with a dose related increase in liver function enzymes. Lungs showed toxic response manifested as emphysematous changes, bronchiolar hyperplasia and peribronchiolar lymphocytic infiltration. n-Hexane effect on the testis was observed in the form of decrease in the average diameter of the seminiferous tubules (310, 260, & 240 µm in groups I, II and III respectively) as compared to control (420 µm). n-Hexane did not significantly affect the serum levels of creatinine, total cholesterol and triglycerides in the exposed animals. This study indicates definite toxic effects of n-Hexane on the brain, liver, lung and testis of the exposed rats.

OS 1.8

EFFECT OF HEAVY METAL IONS ON THE OVARIAN HISTOARCHITECTURE AND SUBSTRATE ENZYME RELATIONSHIPS IN CHANNA (TELEOSTII).

S.B. Lall.

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The effect of sub-lethal doses (predetermined by LC₅₀ tests) of lead nitrate, cadmium salts and zinc sulphate was examined in case of air-breathing *Channa punctatus* during breeding season. Profound degenerative changes were noticed in the ovarian cell types particularly previtellogenic oocytes. Vitellogenic oocytes manifested vacuolation indicating thereby the interference caused by the aforesaid ions on the vitellogenic process. Histoarchitectural changes were correlated with significant changes in the histochemical profile of protein, PAS-positive substances, sudanophilic lipids, lysosomal hydrolases such as acid-, and alkaline phosphatases and mitochondrial oxidoreductases such as lactate and succinate dehydrogenase. Δ^5 -3 β -hydroxysteroid dehydrogenase profile was also very much perturbed. Histochemical data related well with the biochemical estimates of total protein, triglycerides, glycogen, acid- and alkaline phosphatase and lactate dehydrogenase.

Bioremediation

OS 2.1

MICROBIAL AND ENZYMATIC DETOXIFICATION OF TOXIC ORGANO-PHOSPHATES

Krishna S. Rajan and Stephen Mainer

IIT Research Institute, Chicago. IL 60616 USA, and Cheryl Schreiber and Francis C.G. Hoskin, Illinois Institute of Technology, Chicago, IL 60616 USA.

The objectives of this research is to explore biological approaches for the destruction of toxic organophosphorus compounds. Detoxification of the toxic organophosphate, malathion, by three fungal species, viz., *Aspergillus niger*, *Aspergillus flavis*, and *Penicillium funiculosum* has been investigated in growth experiments followed by interactions with their respective cell- free extracts. Within a 24- hour period, *Aspergillus niger* reduced the concentrations of malathion by 81%, *Aspergillus flavis* by 39%, and *Penicillium funiculosum* by 75%. Similarly, studies have been undertaken on the enzymatic detoxification of toxic organofluorophosphonates such as diisopropylphosphorofluoridate (DFP), 3,3- dimethylbutylmethyl phosphonofluoridate (DIMEBU) and pinacolyl methylphosphonofluoridate (SOMAN) by the enzyme, DFPase, derived from thermophilic (*Bacillus sterothermophilus*, PM-14-2) and *Escherichia coli*(ATCC-25922) bacteria and from squid hepatopancreas tissues (*Lolligo peallii* and *Lolligo opalescens*). The activities of the DFPase preparations ranged from 2-4 μ moles /minute.mg protein to 25 μ moles /minutes.mg protein . Material- bounds toxic agent (250-500 mg) was catalytically detoxified (100%) by using 100-120 μ g of the enzyme. Results of studies on the stabilization of the enzyme through lyophilization and immobilization are presented and discussed in terms of its potential for field application.

OS 2.2

RECYCLING OF PLASTIC MATERIALS CAUSING POLLUTION

A.B. Moustafa

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There are some plastics that cause pollution when rejected after being used. Some of these plastics can be recycled by being added in a small percentage from 5 to 10% to the vergin plastic material on condition that they do not have any bad effect on the physico- mechanical properties of the finished product; this usually takes place in plastic factories in the form of plastic parts obtained as a result of trimming the excess parts that are not wanted in the finished fabricated thermoplastic articles, made of polyethylene, polypropylene, polystyrene, polymethylmethacrylate and other thermoplastic materials. The scrap of the polymer whose monomer contains an assymetric carbon atom in its structure such as poly(methylmethacrylate) is thermally degraded to give the corresponding monomer in high yield more than 95% . The

produced monomer is subjected to further purification by fractionation using a suitable fractionating column, of efficient number of theoretical plates. From the obtained monomer, other monomers such as ethylmetacrylate, and butylmetacrylate can be prepared by transesterification. On the other hand, there are other polymers such as polystyrene that can be subjected to thermal degradation to give the starting monomer which is styrene in a low yield which amounts to 41% in addition to toluene which amounts to 2% in addition to a residue which contains a mixture of dimers, trimers, and tetramers with some remaining high polystyrene whose molecular weight is dependent on the degree of devolatilization.

OS 2.3

FACTOR EFFECTS ON THE REMOVAL OF Cr (VI) BY FUNGAL BIOMASS

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Factors effecting chromium (VI) removal by *Rhizopus nigricans* and *Aspergillus niger* NRRL 595 biomass were conducted to determine the environmental conditions that would speed up this process. The rate of Cr (VI) removal from solution proceeded rapidly and it appeared to be virtually complete during the initial 5 min. of incubation of the biomass with chromium solution and then very slowly increased by time. Chromium removal from solution by the biomass was slightly affected by the change in temperature (30 to 60°C). Chromium removal from solutions increased in the first 5 min. in the pH range from 2 to 5 and after that the rate of increase became slower. The amount of Cr (VI) removed, increased as the initial concentration increased. The amount of chromium per g dry biomass decreased with increasing concentration of fungal biomass. On the other hand , the total amounts of chromium taken up by the fungal biomass increased progressively with increasing biomass concentration. When the concentration of both *A. niger* and *R.nigricans* biomass was 3.0 g wet weight, about 65% and 76% Cr(VI) initially applied was taken up by the biomass. Chromium removal from mixed metals solution (containing equal concentration, 100 ppm of Cr, Mn, Fe, Co, Ni, Cu, Zn and Cd) by fungal biomass was dropped from 63% to 37% in case of *A.niger* and from 64% to 45% in case of *R. nigricans* biomass. In addition to the removal of chromium, the biomass of either organism removed considerable amounts of Mn, Fe, Co, Ni, Cu, Zn and Cd.

OS 2.4

DETOXIFICATION OF Cr (VI) FROM SOLUTIONS BY USING FUNGAL BIOMASS

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Among 10 species of fungi, *Rhizopus nigricans* and *Aspergillus niger* NRRL 595 were superior in the removal of chromium (VI) from chromium solutions, about 44% and 35% of 300ppm Cr (VI) solution were removed within 30 min., respectively. Chromium (VI) was highly toxic to the growth of *Rhizopus nigricans* and *Aspergillus niger* NRRL 595 when grown on liquid media containing increasing amounts of the metal. The 50% growth inhibition occurred at 30 and 60ppm Cr(VI) respectively. The fungi were trained to Cr (VI) on PDA or modified czapak agar media by adding of progressively increasing amounts of Cr (VI). After 25 days and five transfers, the 50% growth inhibition was 45 and 74ppm for both trained *R.nigricans* and *A. niger* NRRL 595, respectively. The removal efficiency of chromium from chromium solutions ranged from 25 to 300ppm by non- trained (original) strains was higher than those of trained strains, suggesting the deficiency of some constituents of the trained fungal cell walls. Fungal biomass was treated prior to contact with chromium solutions by several treatments, then the removal efficiency of chromium was evaluated. Cell wall-related biopolymers were tested for the removal of Cr (VI) from chromium solutions. Cellulose and cellulose derivatives and chitosan were active in Cr (VI) removal from solutions. The simplest and cheapest method of recovering surface bound metal from microbial biomass is to elute the chromium (VI) from the surface by diluted sodium bicarbonate, sodium carbonate or nitric acid. The use of *R. nigricans* and *A. niger* biomass seems to be quite feasible in the removal of chromium from the industrial effluents by 87.5% and 80%, respectively.

OS 2.5

DEGRADATION OF LINDANE BY SOIL MICROORGANISMS EVALUATION OF INHIBITORY EFFECT ON MICROBIAL ACTIVITY USING RADIORESPIROMETRY

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The degradation of U-¹⁴C- lindane in two types of Egyptian soil was studied for three months under laboratory conditions. The rate of mineralization of lindane was slow. Evolution of ¹⁴CO₂ increased with time and amounted to 3.5- 5.5% of the initial concentration within 90 days. At this period both soil types contained about 88% of the applied radiocarbon; 33- 37% of the initial dose being bound to the soil. The methanol ¹⁴C- extractables showed by TLC and HPLC analysis the presence of lindane as main product together with traces of minor metabolites. Moreover, the effect of different applications of lindane on the activity of soil microorganisms has been evaluated, using the principle of radiorespirometry. By using U-¹⁴C - glucose as substrate, low concentrations showed an initial suppression of ¹⁴CO₂ evolution. At a dose of 10ppm a significant inhibition of soil microbial activity determined by ¹⁴CO₂ evolution - was observed.

OS 2.6

REMOVAL OF SOME ORGANOPHOSPHORUS AND SYNTHETIC PYRETHROID INSECTICIDES BY ALUM COAGULATION.

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Samples of distilled water spiked with ten mg/l of two organophosphorus insecticides, namely cyanophos and pirimiphosmethyl and two synthetic pyrethroid insecticides, namely fenpropathrin and cyfluthrin were treated in laboratory experiments with aluminum sulphate "alum" to investigate the effect of coagulation on the removal of these insecticides from drinking water. The combined effect of coagulation and chlorination on the removal was tested. The results of the study suggested that removal of insecticide residues was expedited with increasing the alum dose. Also, it was found that pH was the most variable, where the removal was increased by increasing the pH from 4-6 and then decreased from pH 6-8. The data indicated that the removal was affected by the combined method of coagulation and chlorination.

OS 2.7

REMOVAL OF CYANOX, ACTELIC, DANITOL AND CYFLUTHRIN INSECTICIDES BY CHLORINE OXIDATION.

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Removal of Cyanox (0-4-cyanophenyl 0,0- dimethyl phosphorothioate) (I), actellic[0-(2- diethylamino-6- methyl pyrimidin-4- yl) 0,0- dimethyl phosphorothioate] (II), danitol [(RS)- cyano-3-phenoxybenzyl - 2,2,3,3- tetramethyl cyclopropane carboxylate](III) and cyfluthrin [cyano (4-fluro-3-phenoxy phenyl) methyl-3-(2,2-dichloroethyl)-2,2- dimethyl-cyclopropane carboxylate] (IV) from drinking water at levels of 10ppm was studied by using chlorine or chlorine dioxide. Effect of time of contact, oxidant concentrations (2.5 and 5ppm) and pH (3.5, 7.0 and 8.8) on chlorine was investigated. Data cleared that , at alkaline pH, Cl_2 & ClO_2 were more effective for removing these insecticides from drinking water than at acidic pH. Also, it was found that at pH 7.0 and time of contact 180 minutes, ClO_2 (5ppm) removed 45, 47, 25 and 27.5%, while Cl_2 (5ppm) removed 36, 38, 20 and 22.5% of I, II, III and IV, respectively.

OS 3.1

TRANSPLACENTAL TRANSFER OF CADMIUM AND ITS TOXIC EFFECT ON THE EMBRYO- FOETAL DEVELOPMENT IN RATS.

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Cadmium sulfate at dose level of 20 mg/kg was administered by stomach tube from the 6th to the 19th day of gestation. The concentration of cadmium in maternal sera and fetal whole carcass at the 20th day of gestation was measured by atomic absorption spectrometry. Foetuses were examined for any morphological, visceral or skeletal abnormalities. In addition, the physical and behavioral developments of rats in the early postnatal life (from birth to weaning) were evaluated. The results demonstrated that cadmium level in maternal sera was high and was transferred via the placenta to the foetuses in a moderate amount. Postimplantation death, stunted growth, skeletal malformations specially incomplete ossification, and visceral anomalies mainly in kidney, lung and heart were recorded. The postnatal study revealed increased mortality during the first two weeks after birth, retarded growth, and delayed incisors eruption and eye opening. It was concluded that cadmium passes through the placenta inducing serious teratogenic effects in the foetuses and produces dangerous effects in the offspring in the early postnatal life.

OS 3.2

BIOLOGICAL EVALUATION OF AMMONIATED AFLATOXIN CONTAMINATED CORN IN PREGNANT RABBITS

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Treatment of an aflatoxin contaminated feed with ammonia under atmospheric pressure (AP) and biological evaluation of decontamination reaction products are included in this paper. Four groups of female pregnant rabbits were used in 2 trials. Rabbits at early pregnancy (E) were assigned to 2 groups in trial 1, a control group (EC) and a treated one that received aflatoxin contaminated diet which had been ammoniated under atmospheric pressure (E/AP). In trial 2, rabbits at mid pregnancy (M) were divided into 2 groups, a control group (MC) fed on a control diet and, a treated group that fed on the decontaminated diet (M/AP). Rabbits in (E/AP) and (M/AP) groups succeeded to complete pregnancy accompanied by normal parturition and alive offsprings. No mortalities were recorded among treated rabbits. However, postmortem examination of sacrificed rabbits revealed pathological changes in the lungs and uterine horns. Progesterone hormone level was not significantly affected in treated rabbits, while levels of cortisol, blood metabolites and enzymes showed mild variations.

OS 3.3

EFFECT OF PERINATAL LEAD EXPOSURE ON THE FUTURE OF SOME REPRODUCTIVE ASPECTS IN MALE RATS.

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Sprague Dawley male rats were exposed to 0.1% lead acetate in drinking water during the last week of fetal life and the first week of lactation. Other group of male rats was considered as control. A significant decrease in body weight gain and an increase in the mortality rate were observed among the males exposed to lead. The anogenital distance was significantly longer in the exposed males before and after puberty. Delay on the onset of puberty was observed in the lead exposed rats. Although the fertility was not affected, abortion was recorded in 20% of the females mated with lead exposed males. Sperm motility and count were significantly reduced and sperm head abnormalities were significantly higher in lead exposed rats. Slight nonsignificant decrease in testicular weight and an increase in prostate weight with unexpected significant higher level of plasma testosterone was estimated in 160 days old lead exposed rats. The results indicated that perinatal exposure to lead would disturb the male reproductive performance in the adulthood.

OS 3.4

TESTICULAR BIOACTIVATION OF ACRYLONITRILE (VCN)

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Acrylonitrile (VCN), an industrial chemical, is used in the synthesis of plastics and fibres. It has been found in car exhaust, cigarette smoke, drinking water and food products. The present work examines its mechanism of testicular toxicity. In testicular centrifugal fractions, the metabolism of VCN to cyanide (CN⁻) was highest in the microsomal fraction and required NADPH for maximal activity. The biotransformation of VCN to CN⁻ was characterized with respect to time, microsomal protein concentration, pH and temperature. The Vmax of the reaction was 232.5 pmole CN⁻ / mg protein /min and the Km was 135.1 µmole VCN. Flushing the microsomes with CO, addition of SKF 525-A or addition of benzimidazole to incubation mixtures inhibited VCN metabolism. Activation of VCN to CN⁻ was increased in microsomes obtained from phenobarbital - treated rats (127.9% of control). Addition of glutathione, L - cysteine, D - penicillamine or 2 - mercaptoethanol enhanced the release of CN⁻ from VCN. These findings indicate that VCN is metabolized in the testis via cytochrome P 450 - dependent mixed - function oxidase system.

OS 3.5

POSTNATAL DEVELOPMENTAL EFFECTS OF HEPTACHLOR IN RATS

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Xenobiotics enter various organs during pregnancy and into fetal tissue via the placental barrier and milk. These pesticide residues could affect the fetal development either at the somatic or genetic level and manifest as developmental abnormalities. Haptochlor, an organochlorine pesticide and a teratogen, was used to study its effect on the postnatal development in rats. The mothers were treated with the pesticide from 14th day of gestation and their newborns were treated two weeks postnatal by at 1/8th , 1/4 and 3/5th LD50 dose levels. The general, neurobehavioural development and residue pattern was examined. Hapatochlor did not interfere with the general developmental milestones, but affected some of the neurobehavioural aspects. Of the various behavioural tests performed, the placing response and learning ability were affected. There was decline from 91 to 19% in the placing response and from 80 to 20% in the learning ability resulting in the "hyperactive syndrome". A significant dose dependent increase in pup mortality was observed from 24 to 100%. Residue analysis indicated the presence of the parent molecule haptochlor in the placenta and milk. Hapatochlor and its metabolites were detectable in the fetal tissues. However, interestingly epoxide was not present in the placental tissue while it was detectable in the fetal heart. Fetal tissues are known to be capable of degrading the recalcitrant molecules. The fetal ovary had high concentration of haptochlor. The increase in pup mortality could be due to the high epoxide levels in the heart. The details of the various tests and effects are discussed in the paper.

OS 3.6

CHROMIUM (CR) INDUCED CHANGES IN THE OVARIAN ACTIVITY OF SKIPPER FROG *RANA CYANOPHLYCTIS* (Schn.).

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The present study deals with the impact of chromium (Cr) on the ovarian activity of *R.cyanophlyctis*. As the intermediate trophic member of the food chain, this species plays a vital role in the control of pest population and hence needs careful preservation in its habitat free from pollution. The gonosomatic index (GSI), percent changes in different stages of oocytes and histology of the ovary of untreated frogs were found to be normal. The combined exposure to Cr (5.8 and 17.4 mg/l) and temperature (15 and 35 °C) resulted slight decrease in the GSI values as compared to control and no noticeable change in the recovery of GSI was observed after the Cr treatment was withdrawn. Treatment of frogs with both the concentrations of Cr resulted in reduction of FGP number and slight increase in other stages. Cr at low temperature (15 °C) has induced slight increase in number of some stages of oocytes while at high temperature (35 °C) it showed a reverse effects. In Cr injected (100 and 200 µg/Kg body wt.) groups there was a slight decrease in FGP number while other stages like NSGP,

LSGP and AF showed enhancement in their number. Deformities of oocytes and their shape, vacuolation, degeneration of germinal vesicles, fibrosis of cytoplasm and increasing atretic follicles of all stages of oocytes were some of the more pronounced histological changes noticed during Cr exposure periods.

OS 3.7

DEVELOPMENTAL TOXICITY OF THE PESTICIDES HOSTATHION, SUMITHION AND DITHANE M- 45 IN RATS

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The wide spread use of pesticides is usually connected with serious problems of pollution and health hazards. Among the potential hazardous effects of pesticides, foetotoxicity and teratogenicity are of special concern. The effect of hostathion, sumithion and dithane, commonly used pesticides in Egypt, on the developing rat foetuses was studied at two dose levels (1/20 and 1/10 of the LD50). The tested doses were orally given to pregnant rats during the period of organogenesis (from the 5th to the 15th day of gestation). Morphological, visceral and skeletal examinations of the foetuses were used to assess the effect of these chemicals on foetal development. Oral administration of hostathion (4 and 8mg/Kg b.wt), sumithion (25 and 50 mg/Kg b.wt) or dithane M-45 (200 and 400 mg/Kg b.wt) to pregnant rats caused foetal resorption by 12.99% and 16.67%, 13.4% and 19.12% as well as 20.83% and 23.08% respectively versus 4.7% in the control group. Respective percentages of foetal death were 9.09 and 12.5; 7.32 and 11.76 as well as 4.17 and 7.69 versus nil in control rat foetuses. Hostathion, sumithion and dithane caused a marked retardation in the growth of alive foetuses indicated by the significant ($P < 0.01$) decrease in foetal body weight and crown - rump length. Visceral examination of viable foetuses obtained from rats given hostathion, sumithion or dithane showed microcephaly and hypoplasia of the lung. Furthermore, sumithion and dithane caused hydroureter, dilated urinary bladder and enlarged renal pelvis. The most common skeletal malformations were incomplete ossification of the skull, reduced or absence of sternbrae, absence of xiphoid cartilage as well as absence of digits of fore- and hind- limbs. Conclusively, female rats exposed to hostathion, sumithion and dithane during the critical period of organogenesis showed marked foetotoxicity and profound teratogenic effect. Therefore, great attention must be paid during handling and field application of these pesticides to avoid their adverse effects on the pregnant dams and their foetuses.

OS 3.8

REPRODUCTIVE TOXICITY OF THE PESTICIDES HOSTATHION, SUMITHION AND DIATHANE M-45 IN MALE RATS.

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Oral administration of hostathion (2 and 4 mg/Kg), sumithion (25 and 50 mg/Kg) and diathane (200 and 400 mg/Kg) caused a marked decline in male rats fertility index (72.24% and 58.33% ; 63.9% and 74.22% as well as 69.47%, respectively versus 91.78% in control). The percentage of spermatozoa abnormalities as well as dead sperms percent were increased significantly ($P < 0.01$). Furthermore, hostathion and sumithion in both doses significantly, ($P < 0.01$) decreased the weight of testes, epididymides, seminal vesicles and prostate mostly after 60 days of treatment. Meanwhile, the fungicide diathane significantly ($P < 0.01$) increased the testes and epididymides weight after 30 days and mostly with larger doses due to oedema. Serum testosterone level was significantly ($P < 0.01$) decreased with both doses of pesticides tested. Therefore, great attention should be paid during field application of these pesticides to avoid their possible adverse effects on male reproduction in farm animals and occupationally exposed humans.

Drug Toxicology

OS 4.1

INDUCTION OF CHROMOSOMAL ABERRATIONS ON THE SOMATIC AND GERM CELLS IN MICE TREATED WITH PRAZIQUANTEL.

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Praziquantel has a broad spectrum in the treatment of schistosomiasis. The induction of chromosomal aberrations in the bone marrow (as somatic cells) and in the spermatocyte (as germ cells) was used to evaluate the mutagenic effect of praziquantel in mice 8 weeks post- *Schistosoma mansoni* infection as well as in non- infected ones. *S. mansoni* infection caused an increase in the chromosomal aberrations in bone marrow and spermatocyte cells. Praziquantel treatment induced marked changes in the percentage of aberrations in both somatic and germ cells, whereas the mutagenic effect was reduced and returned to the control value after 28 days. These data reflected the mutagenic habitate of praziquantel through the first two weeks of its administration in its effective dose.

OS 4.2

USE OF GLYCOSYLATED LIPOSOMES AS CARRIERS OF MESO-2,3-DIMERCAPTOSUCCINIC ACID (DMSA) IN THE TREATMENT OF CADMIUM INTOXICATED MICE

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Cadmium toxicity leads to its strong binding to metallothionein and storage in hepatocytes intracellularly making it inaccessible to hydrophilic chelating drugs for detoxification. An attempt was, therefore, made to mobilize cadmium from these sites by administering DMSA encapsulated in liposomes composed of phosphatidyl choline and cholesterol (PC/Chol) or PC/Chol /phosphatidyl ethanolamine (PE) anchoring galactose to cadmium exposed mice. Efficacy of DMSA encapsulated in PC/Chol/ PE-gal.liposomes was better than that given through PC/Chol. liposomes which in turn was better than free DMSA in removing cadmium from the body of preexposed animals. Results of lipid peroxidation and glutathione levels in liver also favoured this order. Modulation of liposomes used as carriers of chelating drug could thus be helpful in developing a suitable protocol for the treatment of cadmium intoxication .

OS 4.3

STUDIES ON LITHIUM -PILOCARPINE NEURO-TOXICITY IN RATS.

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An attempt to establish an appropriate animal model of status epilepticus (SE), and also to study the role of various neurotransmitter systems in SE. Administration of lithium chloride, (3 mg/ kg., i.p.) followed 21h later by pilocarpine (30 mg/Kg, S.C.) in rats induced SE. The animals exhibited cholinergic symptoms, facial seizures, followed by rearing and fore limb clonus terminating in death within 24h. While the cholinergic symptoms were sensitive to atropine (2-10 mg/Kg, i.p.), diazepam (5mg/Kg,i.p.) and phenobarbitone (50 mg/Kg,i.p) offered full protection against onset of SE, as the mortality was reduced. The effect was dose dependent . However, the above drugs when given after 30 min of initiation of SE were unable to interrupt the seizure activity. Concurrent administration of diazepam and phenobarbitone exhibited a potentiation. Involvement of excitatory amino acid system was also studied with MK-801. The SE induced by this model was compared with the SE induced by Kainic acid (10 mg/Kg, s.c.) and high dose of pilocarpine (400mg/Kg, i.p.). The reproducibility, prolonged nature and acute cytopathological studies further indicated that lithium -pilocarpine is a potential model for SE.

OS 4.4

ACUTE POISONINGS WITH DRUGS OF ABUSE

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The Kraków Centre apart from high quality medical care to poisoned patients, diagnostic and medical consulting activities (poison information, rapid laboratory analysis) also provides analysis of morbidity and mortality rates due to toxic exposure. A longitudinal epidemiological analysis conducted all the time in the department of toxicology CMUJ has shown a considerable increase of drug overdose resulting in acute poisonings among the drugs abusers of Krakow adult population. The aim of the study was to evaluate the structure and the kind of drug of abuse being the most common cause of acute intoxication. In the period from June 1994 to June 1995, 2159 patients were treated at the department because of acute poisoning with chemical compounds, 51% of them were drug- induced poisonings. This group comprised 48 women and 58 men (mean age was 32 years). Drugs identification was performed using immunoassays Triage tests by Merck, and then the qualitative and semiquantitative determination were made on the Merck vitalab Eclair using fluorescence polarisation. The most frequent resulted from exposure to benzodiazepines (39%) then to opioids (25%) barbiturates (18%), THC (13%), and to amphetamine (5%). Opioids were injected intravenously, while barbiturates and benzodiazepines were injected and/or ingested orally. 111 Symptoms and signs were evaluated regarding to acute, chronic poisonings and withdrawal syndrome. The results presented indicate that only adequate clinical observation, laboratory tests performance and establishing of intoxication state (acute and chronic intoxication or withdrawal) would allow a complete patient - evaluation. Benzodiazepines, barbiturates and opioids were most often the cause of acute poisonings among the adult Krakow inhabitants.

OS 4.5

BLOOD LIPID CONTENTS, PEROXIDATION AND GLUTATHIONE ACTIVITY CHANGES IN RESPONSE TO INDUCTION OF INDOMETHACIN.

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Lipid fluctuations, lipid peroxidase and glutathione peroxidase alterations in blood of albino rats in response to injection of different doses of indomethacin sodium salt (2, 1.5, 1 and 0.5 mg per Kg of the body weight) were studied. All categories were assayed at the end of thirty days of daily intramuscular administration. The elevation of total lipids, total cholesterol, peroxidation level and the inhibition of glutathione activities in blood resulted from the toxicity of the indomethacin. The reduction of glutathione peroxidase activity could be attributed to its ability to detoxify H₂O₂. This

auses the accumulation of H_2O_2 in animal circulating blood and increases H_2O_2 flux, and consequently makes the cells of the organs more susceptible to peroxidative injuries which are facilitated by hyperlipidemia.

OS 4.6

EFFECTS OF CRUDE GARLIC EXTRACT ON MOUSE CHROMOSOMES IN VIVO

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Garlic (*Allium sativum* L.) has been used in Indian indigenous systems of medicine to prevent a wide range of human diseases . The present investigation was undertaken to identify the concentration of the extract and the period of administration which would give the maximum protection against genotoxic effects but will not be appreciably harmful itself. Three concentrations (25 mg , 50 mg and 100 mg/kg body wt.) of fresh garlic were administered daily by gavage to Swiss albino mice for different durations up to 60 days. These concentrations had been observed to protect significantly against effects of known clastogens. The endpoints scored were frequencies of chromosomal aberrations and damaged cells. Bone marrow preparations were made following colchicine-hypotonic-fixative-air drying schedule and stained in Giemsa solution. These parameters were found to be directly dose dependent and after an initial enhancement at 7 days, were reduced following prolonged exposure for 30 and 60 days to the low level observed at 24 hours. Therefore, administration of a low concentration (25 mg/kg body wt.) of the garlic extract daily, is suggested for at least 30 days to obtain the maximum benefit of the extract in protecting against the clastogenic effects of known genotoxicants.

OS 4.7

IN-SITU STUDY ON THE EFFECT OF THIOLA , PIROXICAM AND DILTIAZEM ON THE UTERINE CONTRACTILITY OF γ -IRRADIATED RATS.

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Accidental radiation exposure raises concern of functional modifications in the uterine physiology. It causes tonic uterine contractions and changes in the spontaneous contractile activity in myometrial preparations. In our work, total body γ -irradiation (70, 140 & 210 rads) of non-pregnant female albino rats increased significantly the normal uterine contractility in-situ (measured as frequency / min. and amplitude " μ V/

min"). The protection and treatment from this adverse radiation effect were attempted by using different chemical means. Administration of Thiola (a sulfhydryl agent) in doses of 100 & 250 mg /Kg failed to protect the change in the uterine contractility of γ -irradiated rats (using one shot dose of 210 rads). Also , treatment with piroxicam (a potent prostaglandin inhibitor) in a dose of 2 mg/Kg , before or after irradiation of animals failed to normalize the uterine contractility. However, diltiazem (a Ca^{2+} antagonist) treatment in a dose of 8 mg/ Kg, before or after animal- irradiation, significantly decreased the uterotonic response produced by γ -irradiation; (20.8 % & 61.7 % in the frequency and amplitude of contractions respectively with pre-irradiation treatment) and similarly (21.1 % & 38.6 % respectively with post-irradiation treatment). The results clarified the importance of diltiazem as a tocolytic therapy against the adverse effect of γ -irradiation under the experimental circumstances.

OS 4.8

GENOTOXIC EFFECT PRODUCED BY NORDIHDROGUAYARETIC ACID IN HUMAN LYMPHOCYTES CULTURES.

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Nordihidroguayaretic acid (NDGA) is a polyphenolic compound found in several plants. Recently, it was demonstrated an antimutagenic capacity of NDGA against the effect of several chemicals using the Ames test. To further study this property in mammalian cells, we decided to begin with the characterization of its genotoxic capacity in human lymphocytes in culture, measuring the frequency of sister - chromatid exchanges (SCEs). We used the blood of two female donors, age 23 and 24 years, in an experiment of 72 hr., and tested the following doses of NDGA: 1.1 , 3.6, 6.7 , 13.5 and 27.0 μM . The results were unexpected and showed : 1) a significant SCE increase with all tested doses in one donor and with the four high doses in the other, 2) a dose-response result in both donors concerning the SCE rate, with a maximum increase of 6.5 and 4.57 SCEs, 3) a constant decrease in the rate of mitotic index in relation to the dose , reaching a final value less than half of the control level and 4) a modification of the cellular proliferation kinetics only with the highest dose. Our next step will be to confirm the antimutagenicity of NDGA in *in vitro* and *in vivo* systems.

OS 5.1

CARBON MONOXIDE POLLUTION AND BIRTH DEFECTS

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Carbon monoxide (CO) is one of the most commonly encountered household, occupational, and environmental pollutant. It is produced by the incomplete combustion of carbonaceous material. Every one in modern society is at risk to CO exposure. Experiments were carried out to determine the teratogenicity of CO in mice. The data indicated that CO exposure reduces fertility, increases spontaneous abortions (resorptions), retards fetal growth, and is fetotoxic. The results also indicate that CO exposure leads to concentration related malformation such as microcephaly, microstomia, open eyes and /or open mouth, and brachygnathia. Exposure related skeletal abnormalities were also observed. The research also indicates that CO exposure reduces fetal brain weight / body weight ratio. These findings suggest that CO causes birth defects in mice and cells and tissues of the developing central nervous system appear to be very sensitive to the harmful effects of CO.

OS 5.2

EMERGING TOXICOLOGICAL PROBLEMS IN FARM ANIMALS DUE TO ENVIRONMENTAL POLLUTION IN INDIA

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Increasing trend of toxicosis is recorded in farm animals with ever growing environmental pollution in India. Cross sectional investigations have revealed high prevalence of toxicosis in livestock, mainly due to lead and fluoride. Animals contract acute or chronic toxicity by consuming forage, food and water contaminated from naturally occurring or anthropogenically introduced toxicants. Large number of animals grazing on pasture contaminated from brick work and aluminium factory effluents or drinking water in fluoride endemic zone or fed on diet supplemented with phosphate mineral mixture, developed clinical signs and lesions of fluorosis. Although mortality was low, high morbidity and poor performance of the affected animals caused extensive economic loss to the farmers. Outbreaks of lead toxicosis in cattle and buffaloes were seen near secondary lead smelting units, resulting in heavy death loss and high lead residues in blood and milk of the exposed live animals. Elevated lead levels have been detected in blood and milk of dairy animals from different urban localities in the country. High arsenic and selenium content in natural water and soil in some states is also causing problems to animal health. In general, animals have been

the initial victims of environmental toxicants and monitoring of their health status can be useful to predict ill effects of pollution .

OS 5.3

PERSISTENCE, METABOLISM AND TOXICOLOGY OF PESTICIDES ON CROPS .

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Pesticides are used for better protection of harvest and stored grains against unpredictable losses caused by diseases and pests. Their use is also aimed at improving both quality and quantity and to decrease the extent of vector borne diseases in humans and animals. However, the use of pesticides is accompanied by variety of undesirable environmental effects. The effects include excessive mortality of beneficial insects, reduce production potential in organisms such as birds and fishes, changes in abundance of species and diversity of eco- systems, and production of pesticide resistance in targets and non- target organisms, and residues in air, water, soil and food. To ensure safety from use of pesticides to the consumers, the Indian council of Agricultural Research has sponsored all India Coordinated Research Project on pesticide residues with seventeen coordinated centres located in different agricultural universities and in Indian council of Agricultural Research Institutes. The objectives of the project are i) To study dissipation of pesticides in crops from supervised trials with recommended pesticides and work out safe time- limits between pesticides application and consumption of product. ii) To monitor the pesticide residues in abiotic and biotic components of the environment and iii) To examine the effect of processing of the commodities of decontamination of pesticide residues. The results of researches carried out by All- India coordinated research project on pesticide residues in monitoring, persistence, metabolism and toxicology of pesticides on different crops carried under multi - national trials and under "Good Agricultural practices" will be presented .

OS 5.4

ENVIRONMENTAL EXPOSURE TO LINDANE : TOXICOLOGY INVESTIGATION AND HUMAN HEALTH PERSPECTIVES.

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The pesticide Lindane, which is chemically known as gamma- hexachlorocyclohexane, is one of the eight isomeric forms of a synthetic organic chemical, hexachlorocyclohexane. It is a white solid at room temperature but may evaporate into the air. It is an environmental contaminant that has been identified at approximately 150 of the National Priorities List (NPL) hazardous waste sites in the United States. In

the environment, Lindane is found attached to suspended air particles, in contaminated soil, in vegetation grown from contaminated soil, or in surface water. In the past, U.S. industries used large quantities of Lindane as an insecticide on fruits, vegetables and forest crops. Since the ban on its production and use in the United States in the late 1970's, this compound is mainly imported and formulated for use in the form of dust, powder, liquid or concentrate. Lindane is also used in the United States and in other countries as a medicine to treat head and body lice and scabies. People living near hazardous waste sites might be exposed to Lindane by using contaminated water, by inhaling contaminated air, or by swallowing or touching contaminated dust. People can also be exposed by using medicinal Lindane. Human occupational data and toxicologic studies of laboratory animals suggest that people exposed to Lindane may develop many systemic adverse health effects and, possibly, cancer. Lindane is also known to be a skin toxicant. Many governmental safety and health standards restrict the use of Lindane. The U.S. Environmental Protection Agency and the International Agency for Research on Cancer have classified Lindane as a probable human carcinogen. The presentation will provide up-to-date information on the potential adverse health effects of exposure to Lindane, its chemical toxicokinetics, and its releases to the environment.

OS 5.5

SOME INFORMATION ON INDUSTRIAL AND ENVIRONMENTAL TOXICOLOGY IN CHINA

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Toxicology is the study of adverse effects of chemicals on living organisms. Industrial toxicology and environmental toxicology are the major parts of toxicology. In this paper, some information on industrial and environmental toxicology in China are presented. It includes the historical aspect, the goals and some advances on industrial toxicology, for example, development of new branches of industrial toxicology: research works on special toxicities such as carcinogenicity, teratogenicity and mutagenicity; studies on mechanism of toxicity and toxicokinetics, etc. In this paper some aspects of environmental toxicology in China are described. Besides, the list of the main institutes and medical universities concerning industrial and environmental toxicology in China are introduced, and some main concerned Chinese journals are also presented. In conclusion, it must be emphasized that the international information exchange and cooperation concerning industrial and environmental toxicology should be available and helpful for every person in our world.

OS 5.6

LEVEL OF HEAVY METALS IN WATER HYACINTH AS AFFECTED BY INDUSTRIAL WASTEWATER

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Water hyacinth grows abundantly through the River Nile and its branches as well as the tropical and subtropical regions of the world. Studies were carried out by several investigators indicating the ability and the potential of such plant for accumulating certain pollutants. Attention of environmentalists to study the fate of heavy metals throughout this plant showed significant variation in terms of the surrounding environment. On the other hand, the continuous discharge of industrial wastewater to the water ways can certainly contaminate the environment, namely water, sediment and plant. The present study is discussing the impact of such wastewater on the contamination of Ismailia canal. Particular attention is given to the uptake of heavy metals by the water hyacinth throughout Ismailia canal of variable distances from the point of the industrial wastewater discharge. Results obtained revealed that , the level of heavy metals in plants at the point of discharge are significantly higher than the plants collected at the variable distances. The lowest level was detected at a distance of 5.0 km far away from wastewater discharge point .

OS 5.7

MONITORING OF PESTICIDE RESIDUES IN DRINKING WATER

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Twenty tap water samples were collected from 2 Governorates in Egypt and were analyzed for pesticide residues. The samples were selected to cover a range of exposure to pesticide usage and a variety of water sources (Nile and underground water). Results indicated that 18 samples contained DDT and its metabolites in levels varied between 0.021 and 0.054 ppm. Fourteen samples contained dieldrin in levels varied between traces and 0.004 ppm, while 13 samples contained lindane in levels varied between 0.001 and 0.006 ppm. Endrin was detected in only 12 samples at level varied between 0.001 and 0.015 ppm. Results also indicated that more than 13 unknown compounds were detected. Data show that most of the tested samples from rural areas contained levels of pesticides higher than the samples from urban areas. The level of pesticide residues depends on the source of water. Underground water from depth more than 30m contained traces of pesticides. The highest levels of pesticides were detected in underground water of depth less than 14m. Water samples from Nile water sources contained from traces to 0.001 ppm of pesticide residues.

OS 5.8

ECOTOXICOLOGY OF SUBSURFACE AGRICULTURAL IRRIGATION DRAINAGE: IMPLICATIONS FOR DEVELOPING COUNTRIES

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Subsurface agricultural irrigation drainage is a wastewater with the potential to pollute wetlands and severely impact wildlife populations. Widespread poisoning of migratory birds by drainwater contaminants has occurred in the Western United States and waterfowl populations are threatened in the Pacific and Central flyways. Irrigated agriculture could produce subsurface drainage and wildlife problems in developing countries because several of the factors contributing to toxic drainwater in the Western U.S -- e.g., marine sedimentary basins with soils containing elevated concentrations of trace elements such as selenium and molybdenum, alkaline conditions that favor the formation of water - soluble forms of trace elements, soil salinization problems that require the use of irrigation to flush away excess salts -- also occur in many other arid regions of the world. Proposed agricultural irrigation projects should undergo a technical review to assess regional hydrogeology, evaluate water demand and supply relationships, and determine the potential for drainage problems. Environmental assessments should be made at existing irrigation projects to determine if subsurface drainage is present or could occur in the future. Anticipating and evaluating potential problems will allow alternative irrigation practices to be used for the benefit of agriculture and wildlife.

Genotoxicity & Carcinogenicity

OS 6.1

CHROMOTOXIC EFFECT OF POLLUTED WATER OF LAKE MANZALA ON MITOTIC DIVISION OF *ALLIUM CEPA*, *VICIA FABA* AND *ZEA MAYS*

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The Cytogenetic effects of polluted water on the plants cultivated around and in the islets of Lake Manzala were investigated. Meristematic root tips of *Allium cepa* , *Vicia faba* and *Zea mays* were examined. The pollution reduced mitotic activity and exerted disruptive action on the spindle apparatus, resulting in C - metaphase figures, doubled chromosome number, multipolar anaphase and multinuclei. Chromosomal breakage, stickiness and bridges were also recognized. The frequencies of abnormalities in the three plants indicated that *Vicia faba* is the most sensitive to the chromotoxic action of the polluted water. The concentrations of heavy metals (Pb, Hg, Cd and Zn) were also detected in the sediments of the cultivated areas in the lake.

OS 6.2

GENOTOXICITY OF POLLUTED WATER IN HIGHER PLANTS.I. EFFECT OF TREATED SEWAGE WATER ON MITOSIS AND CHROMOSOMES IN SOME CROPS.

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The effects of irrigation with recycled sewage water at different stages of treatment on mitotic division and chromosomes in root tip cells of *Glycine max*, *Phaseolus vulgaris* and *Gossypium barbadense* are described. The results revealed higher rate of mitotic division and lower amount of chromosomal abnormalities with increased treatment steps of sewage water. The amount of the heavy metals Fe, Mn, Zn and Cu in the roots and shoots of the studied crops was significantly reduced with increased purification of sewage water. The reduction in the amount of these metals is associated with the increased rate of cell division and decreased frequency of chromosomal abnormalities. The reduction in mitotic division and the production of chromosomal abnormalities are associated with anomalous concentration of copper in the root and shoot organs of the tested crop plants.

OS 6.3

GENETIC POLYMORPHISM FOR RISK TO DEVELOP CANCER FROM EXPOSURE TO ENVIRONMENTAL TOXICANTS.

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Polymorphic changes in the GSTM1, CYP2E1 and the CYP2D6 genes are individually associated with increased susceptibility to certain cancers. In the present study, the relationship between genetic polymorphisms for these genes and development of bilharzial-bladder cancer among Egyptian patients was investigated. Our results indicate that the GSTM1 null genotype is more frequently observed in bilharzial-bladder cancer patients as compared to the controls (88.2% and 50%, respectively). The difference is statistically significant with an odds ratio of 7.5 (95% CL= 1.1 - 51.2). In contrast, our investigation failed to demonstrate any difference between bladder cancer patients and controls in CYP2E1 polymorphism as detected by PstI restriction fragment length polymorphism (RFLP). RFLP analysis of the complementary CYP2D6 gene revealed a non-significant increase in the number of

extensive metabolizers in the cancer patients (64.7%) relative to the controls (50%) with an odds ratio of 1.83 (95% CL= 0.37 - 8.97). Our results also show differences in CYP2D6 allelic frequencies between patients and controls indicating a modest trend towards increased risk associated with the homozygous wild type allele relative to the risk associated with the heterozygous alleles. In addition, the frequency of patients harboring the combined CYP2D6 extensive metabolizer and GSTM1 null genotypes was significantly higher than the control (64.7% versus 20%, OR=7.3, 95% CL=1.15-46.1, $p<0.03$). In conclusion, our results indicate that genetic polymorphisms, especially in GSTM1 play a role as a host risk factor for bilharzial bladder cancer.

OS 6.4

GENETIC TOXICITY OF THE PESTICIDES HOSTATHION, SUMITHION AND DITHANE M- 45 IN MICE

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The genotoxic effects of two organic phosphorus pesticides (hostathion and sumithion) as well as the dithiocarbamate fungicide dithane M-45 were assessed employing *in vivo* chromosomal aberration bioassay in mice bone marrow cells. Mice were injected intraperitoneally with 1/20 and 1/10 of the LD₅₀ and the chromosomal aberrations were recorded at 12h post-treatment (for the small dose) and at 6, 12 and 18h post-treatment (for the large dose). Treatment with hostathion at doses of 4 and 8 mg/Kg b.w. caused a significant ($P < 0.01$) increase in the frequency of chromosomal aberrations (4.2% for the small dose as well as 5.8, 4.8 and 3.8% for the large dose at 6, 12 and 18h post-administration, respectively versus 0.67% for the control). The aberrations seen were of the chromatid type (gap, break, fragments and exchange configurations). Sumithion at a dose of 2 mg/Kg b.w given intraperitoneally to mice induced a significant ($P < 0.01$) increase in the frequency of chromosomal aberrations in bone marrow cells, 12h post-treatment (4.4% vs 0.5% in control). Moreover, the larger dose (50mg/Kg) at all treatments (6, 12 and 18 h) induced significant ($P < 0.01$) increase in the frequency of cells with aberrations compared to control (4.4, 7 and 3.8%, respectively vs 0.5%). The predominant types of aberrations met with were chromatid gaps, breaks, fragments and exchanges. Mice treated with the fungicide dithane showed a dose dependent increase ($P < 0.01$) in chromosomal aberrations frequency (3.6 and 6.4% 12h post-treatment with 200 and 400 mg/Kg dithane respectively, $P < 0.05$). Moreover, dithane (400 mg/Kg) 6h post-administration significantly ($P < 0.01$) increased the frequency of chromosomal aberrations (3.2% vs 0.33% in control). The majority of chromosomal aberrations were chromatid breaks and fragments. At 18h post-treatment, dithane was cytotoxic for the bone marrow cells where there was no metaphases observed at all.

OS 6.5

**THE APPLICATION OF GENETIC ALGORITHM IN DISCRIMINATING
NONLINEAR MATHEMATIC MODEL OF POISONISM**

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Genetic algorithm is used to discriminate the nonlinear mathematic model and test its effectiveness with the example of Logistic model, describing the co-effect of poisons, which shows that it operates well and is expected to become an effective tool to discriminate various nonlinear mathematic model in poisonism.

OS 6.6

**ASSESSMENT OF THE ACUTE TESTICULAR CARCINOGENIC EFFECTS
OF ACRYLONITRILE (VCN)**

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Acrylonitrile (VCN), an extensively produced industrial chemical, has been recently reported to interact with testicular DNA and induce unscheduled DNA synthesis. In the present study, the acute carcinogenic effects of VCN were investigated by assessing induced DNA damage and cell proliferation in rat testis. These parameters were observed over a time course extending up to 24 h after a single oral dose of VCN (23.0 mg / kg). DNA damage was maximum at 2 and 4 h after administration. These findings were confirmed electrophoretically. Cell proliferative activity of VCN was examined by determining ornithine decarboxylase (ODC) activity, as well as 5' - bromo - 2' - deoxyuridine (BrdU) incorporation. Maximum induction of ODC activity was observed at 12 h post administration, as it was 35.2 pmol CO₂ / mg protein / 30 min. (control value 2.3). BrdU labeling index was elevated up to 65.0% at 12 h after administration (control value 15.6%). Also, VCN lowered normal testicular glutathione levels by a value of 37.0% at 4 h after administration. These results suggest that exposure to VCN might be a potential carcinogenic hazard to the testis.

OS 6.7

IMMUNOTOXICITY OF ACRYLONITRILE (VCN) ON HUMAN LYMPHOCYTES IN VITRO.

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Acrylonitrile (VCN) is an environmental contaminant. VCN was found to induce immunosuppressive effect in mice. In this work the immunomodulatory effect of VCN was evaluated through the assessment of total glutathione as well as glutathione disulfide (GSSG) contents of human lymphocytes following addition of VCN in different concentrations (10, 20 and 40 μ moles), and at different times of incubation (30, 60 and 120 min). Lymphoproliferative response was also assessed following VCN addition (5, 10 and 20 μ moles) at the same time intervals after stimulation with concanavalin- A (Con-A), phytohemagglutinin (PHA) and Lypopolysaccharide (LPS). DNA damage was also examined following VCN addition. The results revealed that VCN depleted total glutathione content, while increased the GSSG content in human lymphocytes leading to an increase in the GSSG/ total glutathione ratio reaching to 1455.6% and 842.9% of that of control values after addition of VCN (10 μ moles) for 60 and 120 min respectively. Higher concentration of VCN showed similar effects. VCN also inhibited the lymphocyte function following stimulation with PHA, Con- A and LPS as a function of VCN concentration and time of incubation. VCN induced DNA fragmentation that was visualized as ladder appearance on gel electrophoresis indicating apoptosis following lower VCN concentration (5 μ moles) and DNA smearing indicating necrosis following higher VCN concentration (10 μ moles). These results suggest that VCN induces its immunosuppressive effect on human lymphocytes through induction of oxidative stress and / or direct interaction with DNA.

OS 6.8

SUPPRESSION OF CELLULAR IMMUNE RESPONSES IN BALB /C MICE FOLLOWING ORAL EXPOSURE TO PERMETHRIN

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The effects of the synthetic type 1 pyrethroid insecticide permethrin on cell - mediated immunity (CMI) were studied after administration of subtoxic doses by oral gavage. Female BALB /c mice were dosed daily for 10 days with a total dose of either 1%, 0.1% or 0.01% of an oral LD₅₀. Natural Killer (NK) cytotoxic activity was reduced by 42% at the 11% dose level compared to vehicle - treated control mice. Mitogenic responses to allogeneic cells in the one - way mixed lymphocyte reaction (MLR) were also significantly reduced at the 1% dose level. Significant reductions of 63% and 47% in cytotoxic T lymphocyte (CTL) activity were observed at the 0.1% and 0.01% dose

levels, respectively. Oral exposure to permethrin did not produce significant body or spleen weight loss nor did it alter the ability of splenocytes to respond to mitogenic stimulation by concanavalin A (Con A) or lipopolysaccharide (LPS). From these observations, it appears that permethrin has immunotoxic potential and that the CMI is a sensitive target for this effect.

OS 6.9

CARCINOGENICITY STUDY OF BIOTECHNOLOGICAL PRODUCT IN RATS

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Dry hydrolised mud (DHM) was obtained from biochemical plant as an industrial waste in technological process. It was found that DHM is not toxic and can be used as fodder premix for pigs. This study has been designed to reveal the relative carcinogenic risk of this substance. The DHM was administered daily for all life duration. DHM was given mixed with the diet (25 and 50% of total protein was replaced by DHM). Mean survival at the end of the study in all groups was shorter in males than females. A common percentage of animals with benign and malignant tumours in experimental groups was 27.6 and 25.6 and 26.9% in control. No differences in tumour frequency between treated and control animals were detected; in experimental groups 3.2 and 3.8 and 2.2 % in control. Tumour incidence data proved to be higher in female rats. The analysis of our results demonstrates that DHM has not any carcinogenic risk in rats.

Metal Toxicology

OS 7.1

MANGANESE ENTRY INTO THE RAT'S BRAIN INFLUENCED BY MAGNETIC FIELD.

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The aim of the study was to detect the effect of magnetic field on manganese entry into the rat's brain. Experimental group of rats was given intratracheally twice a week for 3 months 0.48 mg of Mn^{2+} per Kg body weight and simultaneously twice a week for 3 months exposed to magnetic field: 10m Tesla, 50 Hz. Each exposure : 1 hour. Control group of rats was given the same manganese doses as experimental group but had no exposure to magnetic field. After the last dose both groups of rats were sacrificed and their brains were analyzed for manganese content. In experimental group of rats positive effect of magnetic field on the increase of brain manganese content in rats was

statistically verified. Visual evoked potentials (VEP) were measured *in vivo* at the end of exposures on some experimental and control rats. Shorter latencies of P1 peak of VEP were found in experimental rats only.

OS 7.2

EFFECT OF LEAD ADMINISTRATION ON SOME BLOOD BIOCHEMICAL PARAMETERS.

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The effect of administration of daily oral doses of lead on various biochemical parameters i.e. GOT, GPT, alkaline phosphatase, urea and creatinine in male albino rats was investigated. Lead was fed in daily oral doses of 333, 666 and 1000µl/100gm body weight for three groups of rats (G1, G2 and G3, respectively) from a solution containing 1000 ppm lead for 20 days. The results indicate that the low dose of lead had a slight effect on GOT and GPT activities, while the highest dose gave a significant effect on GOT and GPT activities. Alkaline phosphatase activity was affected significantly with lead ingestion at the three levels through the experimental period, and may have caused hepatic damage. Concerning the effect of lead administration on plasma urea and creatinine, the obtained results show that their content decreased by the increase of lead dose which suggests tissue failure or post renal obstruction.

OS 7.3

CYTOKINETICS EXPRESSION OF MALE GERM CELL AFTER EXPOSURE TO LEAD, MERCURY, SELENIUM AND CHROMIUM

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Many industrial chemicals have been found to cause male germ cell injury. The predictive assessment exhibited a narrow mechanistic approach by defining the cytokinetics expression and essential target sites in the gametogenesis. The effect of chemicals on male germinal cells was assessed on mature male laboratory animals. Certain biological techniques like atomic absorption spectrophotometry, radioimmuno assay, light and electron microscope were used in the laboratory experiment to evaluate male germ cell expression on exposure to chemicals. Lead exposure causes sperm tail abnormality and showed high lead concentration in human seminal plasma. Lead affects male germinal cells at the level of resting spermatocyte. Mercury affects the process of steroidogenesis and Leydig cells. Spermatogonia and Sertoli cells exhibited maximum deposition of mercury. Complete degeneration in germinal cell was observed after treatment with selenium. Distributions of radioactive selenium ⁷⁵Se were also noted in male reproductive organs. Chromium exposure also causes the germinal cell degeneration at the level of spermatocyte and Leydig cell. GCST may

highlight the safety factors used in extrapolating animal models to human exposure limit for male germinal cell toxicity. Cytokinetics of germ cell expression after exposing to lead, mercury, selenium and chromium exhibited a cell-specific response in male germicides.

OS 7.4

UPTAKE OF ZINC BY TWO FRESH WATER FISHES *LEPIDOCEPHALICHTHYS GUNTEA* AND *LABEO ROHITA*

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Static renewal bioassay (lethal and sublethal) tests were conducted to know the uptake of Zn in the whole body of two fresh water fishes. Experiments have also been carried out with regard to influence of pH and hardness on the uptake of Zn by *L.guntea* during lethal treatment. Studies revealed that during lethal exposures (90 and 110 mg Zn/ l in case of *L.guntea* and 65 and 95 mg Zn /l in case of *L.rohita*) the uptake of Zn in both fishes was slightly higher at lower concentration than at higher level of Zn in the test medium. Sublethal (30 days) studies revealed that, at 5 mg Zn/l exposure, both fishes exhibited an increasing trend in the uptake of Zn as the days were advanced. While a reverse trend was observed at higher level of Zn (25 mg/l) in the test medium. The influence of pH (5.5, 6.5, 8.0 and 9.0) on the uptake of Zn by *L.guntea* showed that uptake was slightly higher in the alkaline medium than in acidic medium. The uptake of Zn by the fish was more in the medium containing 10 and 20 mg Zn/l with 130 mg/l water hardness. Relatively the rate of uptake of Zn was low in soft water than in hard water.

OS 7.5

TOXICITY INDUCED TO PERFUSED HEART BY TWO Cr (VI) COMPOUNDS.

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Chromium is being used in industry for almost two decades. Since then, the adverse effects of its compounds in human health were reported. The effects of perfusion of isolated toad heart with potassium mono - and di - chromate were investigated. Electrocardiogram was recorded before and after application of 1 ml of either K₂Cr O₄ or K₂ Cr₂ O₇ as Cr (VI) (1mM Cr). Several cases of cardiac disorders were noticed after application of any of the two compounds. These cases were represented as different types of arrhythmias, block and S-T segment elevation. Drastic changes of the T wave form were also noticed. Moreover, Cr (VI) compounds also induced

chronotropic, inotropic as well as bathmotropic effects on the heart. The effects noticed indicate direct toxic effects as ischemia.

OS 7.6

EFFECT OF COBALT AND MANGANESE IONS ON LIVER AND KIDNEY OF RAT

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The cobalt and manganese are essential elements and involved widely in biological systems or reactions. But higher intake of these ions were recorded hazardous to the tissues or cells. In present investigation, cobalt and manganese ions are found to cause necrosis, binucleated cells, multinucleated cells, fibroproliferation, glomerulonephritis, pycnosis of nuclei, glomerular damage, damage in the plasma membrane of the distal and proximal convoluted tubules. The lipid contents were recorded higher in hepatorenal tissues. The decreased and diffused activity of some key enzymes like alkaline phosphatase, acid phosphatase, cholinestrace, glucose- 6- phosphatase were also observed. Recently both elements were found to change the nucleic acids, RNA and DNA. Therefore, it is concluded that cobalt and manganese are toxic if taken in higher quantities.

OS 7.7

DERMAL TOXICITY STUDIES OF DENTAL MATERIALS

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Many countries including our own are regularly importing many composite dental restorative materials. These aesthetic materials that can match the shade of natural teeth are prepared over the amalgam or silicate materials. Their use has also increased due to concern regarding long term toxicity of mercury. Because of the high cost and low shelf life a need exists for indogeneous development of such composite materials. As a part of the development of dental materials at our institute, we carried out many biocompatibility studies. The present study is to report the dermal toxicity tests of this material on rabbits as per ADA guide lines. The experiment was designed with 4 groups, consisting of 4 rabbits in each group. Group I, II and III received different concentrations (0.5, 1.0, 2.0 g/Kg) of dental material and group IV as control. All the samples were applied on the dorsal side of rabbit for 3 weeks . Biochemical, haematological analysis were carried out. Necropsied the animal and tissues were subjected for histopathological evaluation. Results of this study showed no significant variation between control and treated groups. Hence it can be concluded that the dental material tested does not elicit unwanted dermal tissue reactions.

OS 7.8

ALUMINIUM : TOXIC OR BENEFICIAL ? A STUDY WITH LAYING CHICKEN

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Aluminium is an interesting element whose toxicity is less understood. Experiments were carried out with laying chicken fed with alum treated sewage effluent as a source of drinking water over an egg - laying cycle. Serum and eggs were collected for various biochemical parameters together with the quality of drinking water. The results indicated that over a period of time, the serum cholesterol levels decreased whereas the egg cholesterol levels increased. Feeding varying doses of pure aluminium sulphate in water also revealed similar trend till the (Al) level was in gram quantities. Only at very high levels the egg shell thickness decreased and the size of the eggs decreased. Does this has any significance when extrapolated to human subjects who consume low levels of Al over longer periods?. Some of these aspects are discussed.

Miscellaneous

OS 8.1

A STUDY ON THE BHC INDUCED NEUROTOXICITY IN *H.FOSSILIS* FROM ASSAM, INDIA.

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The organochlorine pesticides have been widely used in vast agricultural field of Assam, India. These insecticides posed a great threat of toxicological hazard to the aquatic fauna specially the fish. Organochlorine pesticides are known to have neurotoxic effect. In the present investigation the impact of BHC, was studied on brain tissue of *H.fossilis*, the indian cat fish by exposing at 1 ppm, 5 ppm, 10 ppm of BHC in Lab. aquarium for 72 hours along a period of 1 year. The results showed serious cytomorphological damage in cellular and histopathological picture of brain tissue. In 1 ppm test group, neuron cells exhibited marked cytomorphological alteration as normal configuration of the cells converted with irregular distorted and degenerative appearance, 5 ppm test group exhibited chromatolysis, vaculation and partial degeneration showing marked toxic effects. 10 ppm test group marked with demyelination, necrosis and partial loss of cellularity indicated marked cytopathic and histopathic pathological changes. The induction of such pathological changes in the brain tissue with drastic alteration in normal histopattern appeared to be induced by accumulation of BHC residue in brain tissue. Therefore, an attempt has been made for

monitoring BHC residues viz. α, β, τ isomers in the brain tissue exposed to three different sublethal concentrations using GL chromatogram. The mean values of isomers were found to be 1.567 $\mu\text{g} / \text{g}$ in 1 ppm test group, 2.943 $\mu\text{g} / \text{g}$ in 5 ppm test group and 3.751 $\mu\text{g} / \text{gm}$ in 10 ppm test group; which showed that the contamination with BHC induced overall toxic damage to the brain tissue. Therefore, monitoring of pesticide residues in consumers of fish including man should be carried out in affected areas of developing countries like India, where BHC is still used as major pesticide while it is banned in many developed countries.

OS 8.2

EVALUATION OF THE GENOTOXIC AND FOETOTOXIC POTENTIAL OF EMBELIN- AN ABORTIFACIENT, EMPLOYING MICE.

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Oral contraceptives, both hormonal and non-hormonal are being taken by women in India and other countries, as a measure to check the growth of population. The application of the indigenous abortifacient drugs is often based on little or no scientific evidence in regard to their efficiency. There is a need to assess the genotoxic and foetotoxic effects of the abortifacient, as these agents may sometimes fail to produce desired effect. The present study is an attempt in this direction. Embelin is a quinolic compound obtained from the berries of *Embelia ribes* Brun. It is one of the ingredients of the common commercial abortifacient drug, menstrol. The drug in suspension, in different doses was injected intraperitoneally into mouse for varying periods of time. The bone marrow cells from the treated animals were processed to obtain chromosomal preparations. The teratological investigations were carried out by injecting the drug intraperitoneally to the pregnant mice at different periods of gestation. The skeletal anomalies were recorded. Embelin showed a significant reduction in mitotic index and was found to be genotoxic in the bone marrow cells. The embryotoxicity of embelin was evident from the observations of significant reduction in the foetal weight and size. The details of the results were discussed.

OS 8.3

FOETOTOXIC EFFECT OF POTASSIUM CHROMATE (K_2CrO_4) IN SWISS ALBINO MICE.

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The embryotoxic and teratogenic potential of potassium chromate was evaluated by the teratological analysis of mouse foetuses. The test chemical was administered intraperitoneally to laboratory bred Swiss albino mice of both sexes for 30 days.

Teratological scanning of the foetuses born to treated animals revealed a reduction in the number of live implants and litter size. Higher incidence of resorption and dead litters indicated the embryotoxic effect of the test chemical. Malformations, both skeletal and morphological suggest the possibility of potassium chromate (K_2CrO_4) being foetotoxic.

OS 8.4

MYCOTOXINS INDUCED HEPATO AND RENAL CARCINOGENICITY AND ITS CONTROL.

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Citrinin and ochratoxin are hazardous mycotoxins produced by several *Aspergillus* and *Penicillium* species. Oral administration of citrinin (0.25 ml of 50 ppm / animal / day) for 20 weeks alone and in combination with ochratoxin (0.25 ml of 50 ppm / animal / day) to young weanling *Albino* Swiss mice induced significant haematological changes in blood. Histopathological examination of kidneys and liver showed several changes in anatomy of these organs leading to formation of renal carcinoma and hepatic lesions. Analysis of blood as well as histopathological examination of liver and kidney revealed that leaf and berry juice of *Vitis vinifera* had significant positive effect. Recovery up to 40% was achieved through this treatment.

OS 8.5

BIOTRANSFER OF TOXIC METALS THROUGH THE TROPHIC LEAVES OF FOOD CHAIN

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Toxic metals ubiquitously present in our environment find their way into the rivers, ponds, streams and lakes. Carcinogenic metals like chromium and nickel generally get into the environment from the leather industry effluents and manufacture of stainless steel etc. An investigation was conducted on the biotransfer of these metals through the various trophic levels of food chain. Based on our results a model was evolved which explains how these soluble metal ions get into the higher organisms through certain biochemical mechanisms of bioaccumulation and biotransfer. This study points to the fact that caution is required while dealing with environmental metal contaminants. The details of this unique model (biosystem) for useful industrial applications will be discussed.

OS 8.6

STRAND SCISSION IN DNA INDUCED BY URIC ACID IN THE PRESENCE OF Cu (II)

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Uric acid (2,6,8-trioxo purine) is produced in mammalian systems as an end product of purine metabolism and has been proposed as a natural, physiological antioxidant. In the presence of Cu(II) and molecular oxygen , uric acid caused breakage of calf thymus DNA and supercoiled plasmid DNA. Such breakage was considerably enhanced in the presence of visible light. The DNA cleavage did not appear to have any preferred site(s) or sequence(s) for strand scission. Uric acid catalyzed the reduction of Cu(II) to Cu(I) , which was shown to be an essential intermediate in the cleavage reaction. Uric acid also reduced oxygen to superoxide anion and hydroxyl radicals were formed in the presence of Cu(II). The involvement of active oxygen species in the reaction was established by the inhibition of DNA breakage by known scavengers of oxygen radicals. Fluorescence quenching experiments indicated that uric acid is capable of binding to DNA. The uric acid-Cu (II) system was biologically active as it caused inactivation of bacteriophage lambda. Experiments with certain repair defective mutants of *E.coli* indicated that uric acid-Cu (II) mediated DNA damage is repaired in these cells and predominantly involves the po / A pathway.

OS 8.7

HEAVY METAL TOXICITY IN THE ESTUARINE HERMIT CRAB *CLIBANARIUS LONGITARSUS* (DE HAAN)- A. HISTOPATHOLOGICAL INVESTIGATION

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The estuarine hermit crab *Clibanarius longitarsus* is the most ubiquitous organism of Vellar estuary situated in the south east of India (lat.11° 29'N; long. 79° 46'E). Previous study in this environment revealed elevated levels of heavy metals copper and zinc. Therefore, in the present study an attempt was made to asses the toxicity of these metals on the most common organism of this estuary through a histopathological investigation. Metal exposure showed striking histopathological changes in the majority of cells of the hepatopaneas, ovary and gill. The prominent changes effected by metals in the hepatopaneas, ovary and gill are elaborated. In short, the ultimate result of exposure was the loss of integrity of the component cells and their breakdown. Depuration was by and large able to rejuvenate the tissues of all the organs studied in the work at the lowest test concentration .

OS 8.8

TREATMENT OF A PESTICIDE INDUSTRY WASTEWATER IN A DSFF REACTOR WITH CASUARINA SEEDS AS A PACKING MEDIUM

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This study evaluates the applicability of a natural material, casuarina seed, as packing medium in a DSFF reactor treating a pesticide industry wastewater containing toxicants like nitro and chloroaromatics. Ultrastructural examination of this material revealed an extremely porous surface, in addition to a favourable gross morphology. A bench scale anaerobic downflow stationary fixed film (DSFF) reactor of 2 l capacity packed with casuarina seeds was fed with the pesticide waste supplemented with synthetic feed at 0.61 days HRT and influent COD of 600 mg/l for an initial period of 30 days. Rapid start-up, followed by rapid acclimation and high COD removal efficiency was achieved. This is attributed to the ability of the material to immobilize a high concentration of diverse microbial population.

OS 8.9

RESTORATION STRATEGIES OF INDUSTRIALLY POLLUTED RIVER RIHAND BY PHYTOPLANKTON AND MACROPHYTES

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Water quality, phytoplankton diversity, primary production and accumulation of N, P, K, Cd, Cu, Ni, Fe, Pb and Cr in shallow water macrophytes of Rihand River and reservoir at Obra and Renukoot, India were studied under the impact of effluents received from a thermal power plant and a chemical factory (22° 52' N lat. and 83° 5' E long.). pH of the receiving river water increased while transparency, DO, chloride, NO₃ - N and PO₄ -p decreased. Phytoplankton were eliminated in the effluent receiving zone of the river. Chlorophycean members common in unaffected upstream were replaced by Bacillariophycean members. The phytoplankton density, diversity and productivity were reduced. Chloride and PO₄ -p together accounted for 54% (p < 0.01) of the variability to the Bacillariophyta density. Gross and net primary productivities were significantly (p < 0.01) influenced by alteration of the NO₃ - N concentration of the water. Macrophytes showed less nitrogen and phosphorus content in the effluent affected region, while potassium and iron contents increased. Marginal herbs, *Ammannia baccifera* L. and *Polygonum amphibium* L., accumulated high amounts of iron. The results could be appropriately used in the restorative strategies, such as biological harvesting of pollutants, especially heavy metals.

OS 8.10

DEGRADATION OF INDIAN WETLANDS AND REHABILITATION OPTIONS

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Wetland are wide ranging natural and manmade, permanent, temporary or seasonal water bodies or water saturated lands, lentic or lotic, fresh, brackish or saline waters (Ramsar). They have profound ecological and economic importance. In India, wetlands, both natural and man made of different morphometries and sizes are very common everywhere; more so in the states of Bengal, Assam, Orissa, Andhra, Tamil Nadu and Kerala. The burgeoning human population, rapid industrialization, urbanization, expanding agriculture, land fills by garbage, effluent discharges are responsible for degradation of wetlands. Tremendous efforts by the India Ministry of Environment (wetland unit), India Ramsar, Indian Unit of the World Wide Fund for Nature Conservation, are under way in identifying wetlands of national importance, their conservation and management. The authors have made innovative studies on the wetlands and their margins in Surha (listed as of national importance) Lake and Rivers Rihand and Ganga. Quantitative capabilities of marginal vegetation as 'filters' or 'checks' for soil water and chemicals and as heavy metal harvesters have been evaluated. Rehabilitation options are discussed.

OS 8.11

WATER BORNE DISEASES OF BACTERIAL ORIGIN IN RELATION TO QUALITY OF WATER IN A SUBURB OF UTTAR PRADESH, INDIA.

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Waterborne disorders of bacterial origin are one of the major healthy problems faced globally, specially by developing countries like India. The prevalence are largely depending on quality of water consumed by the people. The quality of water in India is still below the standard recommended by W.H.O. which is zero coliform/100 ml of water. The present study was conducted in a suburb of Aligarh distt. of U.P.(India). A total of 1270 persons were selected by paying home visits and followed up for a period of one year. The study revealed that morbidity was higher in standpost group (88.3% while in piped water group it was 51.8%. The average episode of typhoid in both sources of water was one while dysentery had 3 average episodes. The average episodes of diarrhoea was 4 in standpost and 3 in piped water group. In standpost group majority of sample (87.3%) were unsatisfactory as compared to piped water supply. The frequency of typhoid was 1.4%, bacillary dysentery 3.4% and diarrhoea 7.7%. The occurrence of water borne disorders of bacterial origin was common in age groups - typhoid 5-12 years age, bacillary dysentery 1-5 years age, diarrhoea 0-5 years

age. The morbidity rate in standpost group was slightly higher (79.6%). The frequency according to standpost group and piped water group for different diseases were- typhoid 1.1% and 0.7%, bacillary dysentery 2.7% and 2.2% and diarrhoea 6.1% and 5.1%, respectively.

OS 8.12

STUDIES ON CONTAMINATION POTENTIAL OF GROUND WATER (DRINKING WATER) WITH SPECIAL REFERENCE TO ITS MICROBIAL ASPECT IN REWA REGION (CENTRAL INDIA)

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The demand for fresh ground water is on a tremendous increase due to population growth, advanced agricultural practices and industrial usage. This study thus deals with the biotic contamination potential of ground water which is used by 80% of the Indian population. About 200 dug wells, bore well and hand pumps were surveyed for water sampling from August, 1993 to July, 1994 for the assessment of the physico-chemical and microbial analysis with reference to Indian Standards of Drinking. The total solids, total hardness chlorides, sulphate and nitrates of dug well waters were found to be higher in comparison to the hand pump and tube well. Similarly values of iron and sodium were noted higher in almost all the sampling stations of tube and dug wells. Biological indicators are more important to know the extent of contamination. Thus it was observed that all samples were microbiologically contaminated due to the improper sewage and disposal, and unfit for human consumption. In most of the hand pumps, MPN number of coliform, faecal coliform and heterotrophic organisms were found to be higher.

OS 8.13

ORGANOCHLORINE PESTICIDE RESIDUES IN FISHES FROM TAMILNADU COAST, INDIA.

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Organochlorine residues are significant as environmental contaminants because of their stability, bioaccumulative capacity and global occurrence. The gas chromatographic quantification of HCH (BHC) isomers and DDT and its metabolites were made in sixteen species of fish with different feeding habits collected from five major fish landing harbours in Tamilnadu. Elevated levels of DDT were observed than HCH in almost all fishes except *Mugil cephalus*. The β -HCH and p,p'-DDT were predominantly found among HCH isomers and DDT metabolites, respectively. In India DDT was banned for agriculture in 1985 and very small quantity is now being used for vector control purposes. However, higher values of DDTs were recorded due

to their persistency in marine environment or the specific accumulation pattern in marine fishes.

OS 8.14

LEMNA MINOR : A SCAVENGER OF HEAVY METAL

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With expanding growth of cities, freshwater bodies of the region are getting affected due to too much sedimentation of garbage, toxic and non-toxic elements with sewage effluents. Impact of such allogenic loads on *Lemna minor*, a ubiquitous aquatic macrophyte was studied in Shivpurva pond at Varanasi, one of the most ancient cities of the world. This pond receives sewage and solid wastes including heavy metals. *Lemna* was present both at the unaffected control and solid waste affected sectors and was absent in sewage receiving zone. Nutrients and heavy metals like Zn, Pb, Ni and Cd were two to three times higher in plant bodies at solid waste site than at the control site. Biomass and productivity were also higher at control site. *Lemna minor* is a good scavenger of heavy metal and its periodic removal can be used in reducing heavy metal pollution.

OS 8.15

ECO-TOXICOLOGICAL ASPECTS OF STORAGE MOULDS, BIO - DETERIORATION OF CEREALS AND BIOCONTROL.

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Conditions favouring the development of mycotoxins in stored seeds are not well understood. Freshly harvested maize and rice samples were stored in different storage systems at different places under natural conditions. At periodical intervals the samples were collected from these structures and brought to the laboratory for examining seed mycoflora as well as nutritional components of the seeds. Starch, total sugars, reducing sugars, non-reducing sugars, proteins, ascorbic acid, and total keto acids were analyzed at each interval to record changes in their values. Samples were also screened for mycotoxin (aflatoxin) contamination. Different abiotic and biotic variables were monitored for incidence and distribution of toxigenic moulds. Aqueous extracts of some chlorophyllous plants were evaluated for their efficacies in preventing fungal infestations and aflatoxin synthesis during storage. Effective plant extracts were further analysed phytochemically. Identified alkaloid (Indol-3 cyclohexyl propionate) of *Clerodendron phlomis* resulted maximum (74.6%) inhibition in aflatoxin synthesis.

Monitoring Environmental Pollutants

OS 9.1

**ENVIRONMENTAL AND BIOLOGICAL MONITORING TO ASSESS
CADMIUM INDUCED HYPERTENSION AND RENAL DYSFUNCTION**

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Hypertension and renal dysfunction have been closely linked with cadmium exposure. Lack of epidemiological data on this aspect from our country prompted us to study the cause and effect relationship and to suggest a biological marker for early diagnosis of renal dysfunction. The study population consisted of (non smokers, exposed and controls , 20 - 65 yrs , n = 250 each)residing in polluted (SPM 0.757 mg/ m³) and comparatively clean environment (SPM 0.002 mg/ m³), respectively. A detailed personal and family history along with general examination and BP monitoring (weekly X 4 wks.) was carried out as per the perset proforma. Serum creatinine, blood urea,proteinuria , microalbumin , B₂ microglobulin and cadmium were estimated.Cadmium contamination of the air was monitored in SPM. The incidence of proteinuria and hypertension was high in exposed population , the number with proteinuria being higher than those with hypertension. The incidence of microalbuminuria correlated with hypertension and urinary Cd levels while B₂ - microglobulin correlated with proteinuria and urinary cadmium. Serum creatinine and blood urea remained normal . Cadmium in the environment appears to be a possible , causative factor for hypertension and renal dysfunction and urinary B₂ microglobulin could serve as a biological marker for the latter.

OS 9.2

FUNGAL POPULATION IN THE ATMOSPHERE OF ISMAILIA CITY

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Fungal spore populations in the out - and indoor atmosphere of Ismailia have been studied during the period from March 1992 to May 1993. A total of 23350 cfu and 73 species were recorded. In view of frequency *Cladsporium cladosporides*, *Aureobasidium pullulans* and *Aspergillus flavus* proved to be the most abundant. Species counts differ markedly in out - and indoor. Data of out - and indoor by comparison revealed that recorded species could be categorized into three groups as follows a- species showing higher counts in out - than indoor, b- species showing lower counts in out - than indoor, c- species showing approximately equal counts in out- and indoor. Regarding seasonal periodicity, both out- and indoor counts showed the same pattern of change, being high in March- September and low in May- June & December- January.

OS 9.3

IMMUNOTOXICITY OF ACRYLONITRILE (VCN) ON HUMAN LYMPHOCYTES *IN VITRO*.

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Acrylonitrile is an environmental contaminant. It has been found in food, air and water. VCN has been also detected in car exhaust and in cigarette smoke. VCN was found to induce immunosuppressive effect in mice. In this work the immunomodulatory effect of VCN was evaluated through the assessment of total glutathione as well as glutathione disulfide (GSSG) contents of human lymphocytes following addition of VCN in different concentrations (10, 20 and 40 μ moles), and at different times of incubation (30, 60 and 120 min). Lymphoproliferative response was also assessed following VCN addition (5, 10 and 20 μ moles) at the same time intervals after stimulation with Concanavalin - A (Con - A), Phytohemagglutinin (PHA) and Lypopolysaccharide (LPS). DNA damage was also examined following VCN addition. The results revealed that VCN depleted total glutathione content, while increased the GSSG content in human lymphocytes leading to an increase in the GSSG / total glutathione ratio reaching to 1455.6% and 842.9% that of control values after addition of VCN (10 μ moles) for 60 and 120 min, respectively. Higher concentrations of VCN showed similar effects. VCN also inhibited the lymphocyte function following stimulation with PHA, Con-A and LPS as a function of VCN concentration and time of incubation. VCN induced DNA fragmentation that was visualized as ladder appearance on gel electrophoresis indicating apoptosis following lower VCN concentration (5 μ mole) and DNA smearing indicating necrosis following higher VCN concentration (10 μ moles). These results suggest that VCN induces its immunosuppressive effect on human lymphocytes through induction of oxidative stress and /or direct interaction with DNA.

OS 9.4

SUSTAINABILITY OF INDIAN WATER SYSTEMS FOR ORGANO - HALIDES

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Organohalides are non-biodegradable, persist longer, transform into more toxic compounds and some are also generated by the use of chlorine as a disinfectant. The present paper reports the status of water resources in Indian urban areas for organochlorine pesticides and disinfection byproducts trihalomethanes (THMs). The studies indicate contamination of the water sources at Agra, Ahmedabad, Allahabad,

Calcutta, Delhi, Kanpur, Madras, Nagpur and Varanasi with Y-HCH and DDT. The levels to the extent of 12.0 µg/l for Y-HCH and 4.0 µg/l for DDT have been found in intake waters of the treatment plants. Instantaneous THMs (InstTHMs) and THMs formation potential (TFP) were measured during pre- and post- chlorination at the water treatment plants. THMs concentrations in finished water samples were found as: chloroform 0.5 to 18.14 µg/l, median 5.2 µg/l; bromodichloromethane 1 to 12.64 µg/l, median 2.84 µg/l; dibromochloromethane 0.3 to 4.6 µg/l, median 1.4 µg/l and bromoform 0.1 to 7.3 µg/l, median 1.3 µg/l. TFP equivalents of chloroform were measured in finished waters and highest value was found as 123.84 µg/l. Studies reported the presence of organochlorine pesticides and THMs in the waters and recommended for more stringent and continuous monitoring of the water systems.

OS 9.5

INTERTIDAL MOLLUSCS AS A TOOL IN EVALUATION THE STATUS OF MERCURY IN DELTAIC SUNDARBANS, INDIA.

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Levels of total Hg (organic and inorganic) in ten major molluscan species along with the surface sediment; collected from the western sector of Sundarbans during 1993-95; were determined by cold vapour atomic absorption spectrophotometry technique (CVAAS) using a perkin - elmer 2380 AAS equipped with MHS10. The study was carried out to provide baseline data for future environmental quality monitoring programme. Hg levels showed considerable inter- specific and regional variations which reflected dietary concentration and feeding strategy of these animals. A high degree of organ specificity was also registered in the bivalves where gill and mantle exhibited higher Hg accumulation due to the ion exchange activity of the mucus in these organs. The available data demonstrates the potentiality of these shellfishes as sentinel accumulators of Hg and they can be successfully used as sensitive index of pollution. The data also reveals that this coastal zone is alarmingly getting polluted and necessary preventive measures must be adopted to make the best possible use of the available marine resources. A continuous monitoring programme is recommended covering much wider area in order to clarify the present trend.

OS 9.6

IMPACT OF HEAVY METALS RELEASED FROM SOME INORGANIC PESTICIDES ON THE ENVIRONMENT.

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There are increasing demands for crops and food production as a result of the continuous population growth in Egypt. Consequently, a remarkable increase in the use of pesticides and fertilizers in terms of quantities and qualities usually takes place. This can seriously threaten our environment and hence affect the food chain cycle. Some of these pesticides contain certain heavy metals. The uptake of metals by the agricultural crops, the fate of metals via the agricultural soil and the drainage water are question marks. The present study was designed to investigate the level of heavy metals in some pesticides and to study the fate of these metals in the plant, soil and drainage water as a result of using such pesticides. A field study was carried out in an Egyptian village named Etress. The studied pesticides are: mancozeb, Diathine M-45 and Zinc phosphide. The main crop of Etress village is the potatoes. Such plant samples were divided into roots, stems, leaves and fruits. The investigated metals are Cd, Pb, Cu, Zn, Fe and Mn. Results obtained revealed that there is a slight increase in the level of metals in the drainage water as compared with the irrigated water. Meanwhile, noticeable building up of metals in the soil was recorded. The level of metals in the plant samples can be arranged in the following order : Roots > Leaves > Stems > Fruits. The level of metals in the soil can also be arranged as follows : Fe > Mn > Zn > Cu > Pb > Cd. It was then recommended that such pesticides should not widely be used for being an environmental threat as well as a health hazard.

OS 9.7

DETECTION OF ZEARALENONE IN MEAT AND MEAT PRODUCTS

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Zearalenone (ZEN) is a potent toxic agent produced by several *Fusarium* species and known to be a common and wide spread contaminant in cereal grains and animal feedstuffs. Various health problems associated with this mycotoxin have been well documented in domestic animals such as decreased feed intake, infertility, vaginal prolapse and enlargement of the uterus and mammary glands. Consequently, there is increasing concern about the potential health hazard of (ZEN) to humans, not only from direct exposure to contaminated cereal products, but also through consumption of meat derived from animals exposed to (ZEN) contaminated feeds. Twenty samples of

each of fresh meat, frozen meat and meat products of (Luncheon , minced meat, sausage and hamburger) were used . The percentages of positive samples were 15, 20, 15, 10 and 20 % in fresh meat, frozen meat, luncheon, hamburger and minced meat respectively. The average amounts of (ZEN) extracted from fresh and frozen meat positive samples were 3.18 and 2.32 $\mu\text{g} / \text{Kg}$, respectively. On the other hand the average amounts of (ZEN) extracted from luncheon , sausage , hamburger and minced meat were 2.66, 1.96, 2.10, and 3.13 $\mu\text{g} / \text{Kg}$, respectively. The data of the present study clearly indicated that the highest amount of (ZEN) was recorded in fresh and minced meat.

OS 9.8

ASSESSMENT OF SMOKING-INDUCED DNA DAMAGE IN LYMPHOCYTES OF SMOKING MOTHERS NEWBORN INFANTS USING THE ALKALINE SINGLE CELL GELL ELECTROPHORESIS TECHNIQUE.

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The single cell gel electrophoretic (SCGE) technique for detecting the presence of DNA strand breaks and alkali-labile damage in individual cells was used to examine the effect on newborn infants of maternal exposure to cigarette smoke. The levels of DNA damage in the lymphocytes of 21 newborns of mothers with different smoking habits were compared to that in 10 newborn infants whose mothers had never smoked and to 8 newborns whose mothers were passively exposed for at least 40 hours per week in the workplace and home. DNA damage was undetected in lymphocytes of newborns of passively exposed or newborns with mothers of low smoking habit by conditions allowing 40 minutes DNA unwinding and 40 minutes electrophoresis. The mean length of DNA migration in lymphocytes between the newborn of smoking mothers did not show any significance but the % of damaged cells increased with the frequency of smoking when assessed by non-parametric Mann Whitney U test. The results of SCGE were compared with our results published on the same individuals by sister chromatid exchange (SCE) frequency. The results show similar trends with mean measures of DNA damage increasing with frequency and long history of maternal smoking. These observations encourage the application of SCGE as a sensitive and useful technique for quantitating DNA damage in individual cells.

Natural Toxins

OS 10.1

PROBLEM OF NATURAL TOXIN ENVENOMATION IN DEVELOPING COUNTRIES.

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Envenomation by snakes, spiders, marine organism, etc. is a serious health hazard in many parts of the world especially in developing countries which are agriculture based or fisheries based. For example, in Burma (Myanmar) Russell's viper bite causes about 1,000 deaths/ year. In India more than 20,000 deaths/ year due to snake bites were reported. In Sri Lanka, the incidence of snake bite has increased to more than 400 per 100,000 population per year. The many species of land and sea snakes belonging to the families, Crotalidae, Elapidae, Colubridae and Hydrophidae will be described. Medically important scorpions, spiders and centipedes will be described in addition to the problem of scorpion envenomations in Asia, Africa, Middle East as well as south America. Bees, wasps and hornets stings is a common problem in many countries especially tropical countries. Systemic effects, anaphylactic reactions as well as local effects are problems due to these stings. Marine creatures such as the venomous fishes (e.g. sting ray, scorpion fishes, etc), poisonous fishes (e.g. Puffer fish) venomous marine coelenterates and annelids (e.g. jelly fish), poisonous crabs, and dangerous echinoderms, molluscs (e.g. sea urchins, cone shell) also will be discussed.

OS 10.2

EFFECT OF OCHRATOXIN A ON THE HEART RATE AND ARTERIAL BLOOD PRESSURE OF RAT.

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Ochratoxin A (OA) is a mycotoxin produced by certain species of storage fungi of the *Penicillium* and *Aspergillus* genera. OA is actually toxic to different animal species. In addition to being nephrotoxic, it is hepatotoxic and a very potent carcinogenic substance. Its effect on the cardiovascular physiology of animals has not been studied in details. In the present study OA was i.p. injected (800 and 1600 µg/kg B. wt.) into two groups of urethane anaesthetized rats, respectively. Another group was i.p injected with the OA vehicle (0.1 M Na HCO₃) and considered a control group. Heart rate (HR) and arterial blood pressure were recorded for 3 hours following the administration. Significant bradycardia has been obtained half hour after OA administration and sustained up to two hours compared to the control group. Significant depression of arterial blood pressure was established half hour following the administration in both systolic and diastolic blood

pressure. Mean arterial blood pressure was significantly decreased after one and half hours in both treated groups and continued up to 3 hours in case of the higher dose. In conclusion, OA might have a strong effect on the performance of the myocardium and consequently on the arterial blood pressure.

OS 10.3

EFFECT OF ACUTE ADMINISTRATION OF OCHRATOXIN A ON THE ELECTROCARDIOGRAM OF RAT.

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The occurrence of Ochratoxin A (OA) in food and feed is widespread and it is known to be highly toxic to animals. Liver and Kidney are mainly the target organs for OA toxicity. Also, it was reported that a myocardium damage occurs as a result of acute OA toxicity. In this investigation, the effect of this toxin on the electrical activity of the myocardium (ECG) has been studied. Two groups of urethane anaesthetized rats were i.p. injected with two different doses of OA (800 and 1600 µg/kg B.wt.), respectively. A control group was i.p. injected with the OA vehicle (0.1 M Na HCO₃). Electrocardiogram (ECG) was recorded for 3 hours after OA administration by the insertion of subcutaneous electrodes according to the axis of the rat's heart "Lead II". Different ECG parameters were measured to demonstrate the actual effect of OA on this important factors. Significant increase started one hour after administration in the "P-R" interval in both treatments. "Q-T" interval showed slight insignificant increase in case of higher dose injection. Regarding "R" and "T" waves amplitude, they were significantly elevated after 2 hours in both groups and sustained till the end of the experiment compared to the control group. In summary, it is clear that the conductivity and the contractility of the myocardium are highly affected by OA treatment.

OS 10.4

ALBIZZIA ANTHELMINTICA BARK DUST AND AQUEOUS FRACTION: THE ASSESSMENT OF THEIR RESPIRATORY SENSITISATION POTENTIAL IN GUINEA PIGS.

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Guinea pigs were more susceptible to both sensitization and challenge exposures of 100 mg/m³ *A. anthelmintica* bark dust than were animals of the same age exposed to 1% aqueous fraction from *A. anthelmintica* bark. In affected animals, the respiratory rate was markedly decreased and multifocal alveolitis, alveolar haemorrhage and accumulation of inflammatory cell response as well as fatty cytoplasmic vacuolation and necrosis of the centrilobular hepatocytes were observed. The significance of these findings is discussed.

OS 10.5

A BIOCHEMICAL STUDY ON RATS INJECTED WITH THE VENUM OF *ANDROCTONUS CRASSICAUDA*.

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The effect of i.p. injection of single LD₅₀ dose and repeated sublethal doses (1/4 LD₅₀ on each of 4 and 8 consecutive days) of *Androctonus crassicauda* venom on male Sprague Dawely rats were studied after 24 hours of last injection. LD₅₀ dose (0.8 µg/ g.b.wt.) produced significant decrease in the activity of GOT, Na⁺ion concentration, bilirubin, and glucose contents. Repeated sublethal doses (0.2 µg / g. b. wt. for 4 and 8 consecutive days) produced significant decrease in total serum protein, albumin, glucose , hemoglobin and haematocrite%. Significant increases in GOT and bilirubin were also recorded. It is assumed that the venom has great effects on rats metabolic activity represented by such biochemical disturbances.

OS 10.6

HAEMATOLOGICAL AND BLOOD BIOCHEMICAL ALTERATIONS INDUCED BY REPEATED ADMINISTRATION OF *ESCHERICHIA COLI* ENDOTOXIN IN MALE CALVES.

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The effects of multiple injections of *Escherichia coli* endotoxin (1.0 µg / Kg, i.v.) were assessed on haematological and blood biochemical parameters of calves. The administration of endotoxin produced significant pyrexia , respiration and pulse rates, leucopenia , lymphopenia and neutrophillia with greater percentage of immature blood cells. Blood urea nitrogen was significantly reduced ,while blood glucose levels elicited a biphasic response. Serum levels of AST and ALT were significantly elevated whereas the activities of serum LDH, ACP and ALP remained unchanged. There was significant hypozincaemia, hypoferraemia, hypocupraemia, hypocalcemia, hypomagnesaemia and hypernatremia. It has however, no effect on Hb, PCV and serum inorganic phosphorus levels. Results indicated that even in small doses *Escherichia coli* endotoxin induces a marked haematological and biochemical effects in calves.

OS 10.7

AFLATOXIGENIC ISOLATES OF *A. FLAVUS* OF AMBIENT AIR AND POSSIBILITIES OF AFLATOXICOSIS.

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Form the researches carried out at this centre as well as at abroad it is very much apparent that the mycotoxin elaborating fungi remain in dominant form inside hospital wards, Graineries , Godowns and residential places . Artificial exposure to guinea pig, albino rat and rabbits have shown some positive results. For the purpose, a glass chamber was specially fabricated at the centre so as to allow the ambient animal to thrive in air mixed with aflatoxigenic *A.flavus* spores (NRRL-3999). Histopathological studies of the lung , tracheae may reveal some marker or symptom caused. Estimation of mycotoxin level in the blood (peripheral) is also being done . Encouragement extended by Dr.A.V.Costantini , Germany is thankfully acknowledged.

OS 10.8

MYCOTOXINS IN BREAST CANCER PATIENT'S MILK / CORD FLUID AND THEIR FOOD.

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Mycotoxins, like Ochratoxin A and Aflatoxin M₁ has been detected in the breastmilk or cord fluid of some 17% patients (45/263) suffering from breast cancer. The patients were diagnosed by the local physician and confirmed by the cancer specialists centre. Food grains collected from their homes, markets and near by localities bore high degree of aflatoxigenic strains of *Aspergillus flavus* and to some degree of *A.ochraceous* elaborating ochratoxin A. Consumption of such contaminated food grains during pre- and post- pregnancy period might have caused accumulation of mycotoxin residue in the body leading to their transformation and indirect inciting the disease. Capacity of mycotoxin production *in vitro* and quantitative estimation of mycotoxins present in the milk / cord fluid is under progress; TLC technique as suggested by Coker *et al.* (1984) in TDRI manual being employed . Thanks to Dr. Costantini , Germany, for encouragement and accepting the centre as collaborator of WHO-CCMF.

OS 10.9

A RECENT METHOD FOR DETERMINATION OF MYCOTOXIN ZEARELENONE AND ITS METABOLITES IN RATS.

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Zearalenone (ZEN) is mycotoxin possessing strong estrogenic activity when fed to domestic animals. Zeranone is a synthetic derivative of zearalenone which is used to

increase growth performance in beef cattle and sheep. Either of these substances if present in sufficient quantities in the diet could cause many serious problems to our animals, Although overtotoxicosis resulting from ingestion of residue contaminated food products is a relatively uncommon occurrence, the long term health effects from repeated exposure to low concentration of certain chemicals may be of much greater concern. This study was conducted to develop a high performance liquid chromatography method for identification of zearalenone and its metabolites. With validation of the procedure, the minimum detectable concentration for zearalenone in methanol was 4 µg/ml and the retention time was 17.17 min for ZEN, 9.2 min for alpha ZEN, and 6.45 min for beta ZEN. (n = 9 runs). Linearities of the calibration curves were performed in rat plasma. Linearities study revealed that, ZEN was linear in a wide range of concentration in methonal and plasma ranging from 4 µg/ ml to 100 µg/ ml, alpha ZEN 2 µg/ ml to 100 µg/ mL and beta ZEN 2 µg/ mL to 100 µg/ ml.

OS 10.10

EFFECTS OF *BACILLUS THURINGIENSIS* BACTERIA AND SPOR- δ -ENDOTOXINS ON THE IMMUNE SYSTEM OF *BOMBYX MORI* LARVAE.

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Bombyx mori larvae showed great responses against injected *Bacillus thuringiensis* bacteria and spore- δ - endotoxin complex (50 and 100 µg / ml) for different time intervals (2, 4, 6', 12, 18 and 24 hr). Total haemocyte counts (THCs) dropped rapidly after all injections. Differential haemocyte counts (DHCs) also showed many changes. Prohaemocytes (PR) increased in numbers post-all injections while *B.thuringiensis* caused decrease in the numbers of plasmatocytes (PL), granulocytes (GR) and spherulocytes (SP). Coagulocyte (CO) numbers were inconsistent. Spore- δ - endotoxin complex (50 µg / ml) showed decrease in (PL) numbers where all the other types were increased. Concentration of 100 µg / ml decreased PL and GR numbers and increased SP and CO numbers. Phagocytosis and nodule formation reactions were higher after injection of *B.thuringiensis* , then spore δ - endotoxin complex (100 µg / ml) and the reactions were weaker against 50 µg / ml suspension of the Spore- δ - endotoxin complex. Humoral reactions (antibacterial lytic factors) showed reversable directions with cellular reactions as they were stronger against spore- δ - endotoxin complex than *B.thuringiensis* bacteria.

OS 11.1

PERSISTENCE OF CARBOFURAN RESIDUES IN STORED SOYBEANS AND THEIR BIOLOGICAL SIGNIFICANCE

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The degradation of carbofuran on soybeans stored for 30 weeks under conditions similar to those prevailing locally was monitored using a radiolabelled insecticide. After 24 weeks of storage, the maximum percentage of methanol extractables inside the seeds was found to be 50- 60% and only 3-4% of the applied dose was present as bound residues. In addition to carbofuran, the methanol extract contained at least three metabolites. These were detected and identified by chromatographic procedures as carbofuran phenol, 3- hydroxy carbofuran and 3- Keto- carbofuran phenol. Subchronic feeding studies on mice with soybeans having carbofuran residues were conducted for three months at a concentration of 4.5 ppm carbofuran equivalent. The effect on body weight gain, cholinesterase activity and blood chemistry was monitored during the feeding period. A significant inhibition of plasma and erthrocyte cholinesterase activity was observed after 2 and 3 months. Serum transaminases, alkaline phosphatase and blood urea nitrogen were significantly elevated indicating injury to hepatic and renal structures. These results suggest that carbofuran residues can induce adverse biological effects in mice.

OS 11.2

HISTOPATHOLOGICAL CHANGES OF MALE GENITAL SYSTEM OF PATS ADMINISTRED PESTICIDES HOSTATHION, SUMITHION AND DITHANE M-45.

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Histopathological changes of two organophosphorus pesticides hostathion (4 and 8 mg/ Kg b.wt.), sumithion (25 and 50 mg/ kg b.w), as well as the carbamate dithane M-45 (200 and 400 mg/ kg b.w) were studied in male genital system of 90 rats, for 60 days. The results revealed mild testicular degeneration with low doses and moderate testicular degeneration with the high doses of tested pesticides. Epididymal sperm reserves were slightly affected with the low doses but greatly reduced with the high doses of all tested pesticides,. Accessory genital organs were not or mildly affected with low doses and moderately influenced by the high doses as indicated from the decrease of secretory materials in the seminal vesicles alveoli and prostatic acini.

OS 11.3

HAS WARFARIN RESISTANCE DEVELOPED IN EGYPT ?!

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On the basis of the fact that Egypt has been using anticoagulant rodenticides for about 15 years three techniques were effectively used to reveal the present susceptibility of the Norway rat caught from different governorates to warfarin. Feeding a 50 ppm warfarin bait for 6 days caused all the suspect animals to succumb and none were referred to as resistant. However, when coagulation was assessed 24h after a single i.p. injection of warfarin (5mg/Kg) together with vitamin K₁ 2,3 epoxide (1mg/Kg), 2 out of 14 rats from menufiya proved to be warfarin resistant. On the other hand, when coagulation was assessed similarly 24 th after a single oral injection of sodium warfarin (5.4mg/Kg) together with menadione sodium bisulphite (1mg/ Kg), 6 out of 24 suspect animals, again from menufiya, revealed warfarin resistance. The present study claims, consequently that resistance to warfrain was developed in Egypt especially in the governorates where anticoagulants were used intensively, It also seems likely on the light of the present results that the recorded cases of resistance belong to the welsh type.

OS 11.4

CONSEQUENCES OF METOLACHLOR PERSISTENCE OF TREATED AND SAFENED ZEA MAYS ON GIBBERELLINS, GLUTATHIONE, A- AMYLASE, AND GLUTATHIONE S- TRANSFERASE

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Metolachlor residues, contents of gibberellic acid (GA₃) glutathione (Y-L- glutamyl-L- cysteinyl glycine, GSH) and protein, as activities of a amylase and glutathione S-transferase (GST, EC 2.5, 1.18) were investigated in shoots of six-d - old maize seedlings during 8 days following treatment with metholachlor, either alone or combined with naphthalic anhydride (NA), flurazole (FL) or GA₃. Metolachlor induced a significant decrease in GA₃ content and in - amylase activity. NA and FL seemed to lower these decreases while externally applied GA₃relieved this effect. Similarly metolachlor provoked a significant decrease in dry weight and protein contents. The herbicide had no significant effects on dry weight when combined with NA, FL, or GA₃ as well as on protein by the presence of NA or FL, but GA₃ seemed to have no influence. Metolachlor residues progressively accumulated in shoots up to the 4 th day from treatment, thereafter the residues declined. A significant decrease of metolachlor persistence was observed by the presence of NA or Fl but not by GA₃. Comparable significant increases of GSH content were induced by metolachlor or its combinations, moreover FL had a remarkable effect to about 2.2- fold. GST activity was significantly enhanced by metolachlor. This effect was not changed by the

presence of GA₃ while NA or FL appreciably induced 3.2- or 7.2 fold higher than metolachlor - induced GST activity. The results suggest that GA₃ recompensed metolachlor- induced losses of endogenous GA₃ and α - amylase while safeners stimulated the herbicide detoxification .

OS 11.5

A STUDY TO CORRELATE THE TOXICITY OF A PESTICIDE UNDER MALNOURISHED CONDITION BY BIOCHEMICAL ANALYSIS.

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In the present work toxicity of an organophosphorous pesticide eg. phorate has been studied to find out its impact on male, adult, albino rats maintained at various degrees of protein - energy malnutrition. The changes in the activities of phosphatases, transaminases and drug metabolising enzymes of the liver have been studied at 24hrs (acute) and 3 weeks (sub-acute) time period. It was evident from the results that lipid-protein bilayer of the hepatic memberane was affected with the diminution of both protein and lipid contents. The toxicity was more pronounced during sub- acute exposure. The levels of nucleic acids were also lowered during sub- acute toxicity. The transaminases and phosphatases enzymes showed an inhibition in the activity both under acute and sub- acute exposure of pesticide. Reduced activity of N- Demethylase, B- Glucuronidase and unaltered activity of aniline hydroxylase was observed after pesticide exposure under pemcondition. From the foregoing results it could be concluded that phorate had marked effect on the metabolism of liver and the toxicity was enhanced further by PEM conditions in male, adult, albino rats.

OS 11.6

SPECIAL PROBLEMS ASSOCIATED WITH PESTICIDE USE AND ITS MANAGEMENT IN GAZA STRIP

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Gaza Strip is a semi- arid region of roughly 36 5Km² (46 Km long and 6-10 Km wide) which lies on the mediterranean sea, with an estimated population of over 900,000. Its warm climate favors cultivation of many strategic crops including citrus, olives, almonds, grapes, and other subtropical fruits, vegetables and flowers. Gaza Strip is bound to the industrialized countries for exporting their cash crops and importing all production equipment and materials including pesticides and fertilizers. It suffers from catastrophic environment and degraded infra- structure, water shortage, water pollution with high salinity and micro- pollutants, lack of sewage and solid waste treatment, maritime pollution , uncontrolled and heavy use of pesticides, overpopulation and overcrowding, poverty and low standards of living, their deficient economy and infrastructure hinder their ability to regulate efficiently registration of pesticides. Special problems related to the misuse and overuse of pesticides have become widely recognised and documented in recent years . For example internationally suspended, banned and cancelled pesticides which considered mutagenic and carcinogenic are still used in the agricultural environment of Gaza Strip. Its inhabitants are at high risk due to the acute and chronic adverse health effects induced by pesticide exposure under both occupational and epidemiological conditions. This recognition has led to strong public demand for solution in the form of information exchange, assistance in the development of legislation , guidelines on advertising and labelling. These, and other measures have been sought in a variety of international fora Gaza Strip legislations, regulations, regulations technical capabilities, and medical care need to be upgraded to a reliable standard. This is essential for the global welfare because any hazardous pesticides dumped or released in environment in Gaza Strip will not be dissipated but can reappear as residues in imported raw foods or destroying terrestrial and aquatic life, through their transportation within the atmosphere, or in liquid discharges to soil and water bodies international assistance and support are badly needed by United Nations Agencies, mainly WHO, UNEP, FAO, ILO, IPCS, IRRTC, and other relevant international organization .

OS 11.7

ALDRIN ADMINISTERED CHANGES IN HAEMATOLOGY OF ALBINO RATS

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Healthy female albino rats were administrated orally a sublethal dose (1/3 of LD₅₀ value) of 95% Aldrin for 96 hours. A group of 8 rats was kept as control and a group of 32 rats were used as experimental group. Different selected haematological parameters were studied in both groups of animals. From experimental group each time after 24, 48, 72, and 96 hours of pesticide administration , 8 rats were sacrificed and all observations were based on the mean values of 8 individuals. Significant changes were observed in experimental animals. The total erythrocyte count and mean corpuscular haemoglobin concentration declined significantly in the experimental rats as compared to the control ones. However erythrocyte sedimentation rate and mean corpuscular haemoglobin were significantly higher in the experimental rats. It was concluded that oral administration of aldrin causes haematotoxic action to the tested animals.

OS 11.8

CHEMICAL CONSTITUENTS AND PESTICIDE RESIDUE LEVELS IN HUMAN, COWS AND BUFFALOES MILK

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Milk and its products are a main constituent of the daily diet especially for vulnerable groups such as infants, school- age children, pregnant lactating women and old age. A total of 128 samples were collected at random from different sources and sites in Egypt. Seven samples were human milk, 67 were cows milk and the rest were buffaloes milk. All the tested samples were analysed for the detection of fat, sugar protein and ash. Data indicate that there was a great difference in their constituents. The percentage of fat in human milk varied between 3.67- 3.79% while it was 3.89- 4.12 and 7.58- 7.98 for cows and buffaloes samples, respectively. Buffaloes milk headed all the tested milk in its content of protein (3.98- 4.01 %) , followed by cow milk (3.27- 3.31) and by human milk (1.89- 2.03 %). Human milk headed all the other tested milk in its sugar content (6.19-6.21 %) followed by buffaloes milk (5.01- 5.19 %) ,and by cow milk (4.99- 5.09 %). The total content of ash was 0.68, 0.31, 0.78 % for cow, human and buffaloes milk, respectively. All the tested samples of buffaloes and cow milk contained DDT and its metabolites, lindane, endrin, dieldrin, while only 85% of the tested human milk samples contained lindane, DDT and its metabolites.

dieldrin, and endrin. The presence of these residues varied between traces to 11.9 ppm, in buffaloes and cow milk, while the maximum residue level was 1.26 ppm in the case of human milk. The level of pesticide residues was related to the fat content of the tested milk. Buffaloes milk headed all the other tested milk in its content of pesticide residues followed by cow and finally by human milk .

Preventive & Regulatory Toxicology

OS 12.1

L-HISTIDINOL ENHANCEMENT OF CISPLATIN THERAPEUTIC INDEX AGAINST EXPERIMENTAL EHRlich ASCITES CARCINOMA

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The antitumor activity and host toxicity of cisplatin and /or L- histidinol was studied on Ehrlich ascites carcinoma (EAC) experimental tumor. L- histidinol (1-4 mM) caused significant potentiation of cisplatin (1-20 μ M) cytotoxicity against cultured EAC cells in a concentration - dependent manner. By means of tritiated thymidine incorporation as criterion of the rate of DNA synthesis, L- histidinol (2mM) was shown to augment cisplatin cytotoxic effect through further inhibition of DNA synthesis. Cisplatin (2,7 & 14 mg/Kg, i.p) co- administration with L- histidinol (250 mg/ Kg, 5 i.p injections every 2 hrs starting 2 hrs before cisplatin injection) greatly improved therapeutic index of cisplatin in EAC- bearing female Swiss albino mice. The combined regimens showed increased average life span & number of long term survivors and reduced tumor burden of mice. Moreover , L- histidinol markedly protected the tumor- bearing mice against cisplatin dose- limiting toxicities (nephrotoxicity and myeloid suppression). The study suggests that L- histidinol not only enhances the therapeutic efficacy of cisplatin, but also ameliorated tissue host toxicity of cisplatin and possibly indicating a potential increase in the utilization of cisplatin in clinical cancer chemotherapy.

OS 12.2

ON IMPROVING WHOLE EFFLUENT TOXICITY DATA ANALYSIS & INTERPRETATION IN REGULATORY COMPLIANCE.

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In current regulatory practice, whole effluent toxicity data are analyzed on a test - by - test basis without adjustment for between test variability. Recently, statistical models which include both the intra - and inter - test variability have been proposed and

applied to reference toxicant data. These models were shown to be more appropriate in controlling Type 1 error than the current approach. The solution offered was to first estimate an adjustment to the error variance with reference toxicant data and then apply the adjustment to the data from a given effluent test. We examine the proposed adjustment issue further. Specifically, we present results from several laboratories and species on the possible ranges of adjustments needed in effluent & reference toxicant data. It turns out that this problem has a theoretical solution. We give the relationship between the ratio of the dose - by - test interaction variance component and the error variance component as it relates to the inflated Type-1 error. This result eliminates the need for estimating the variance components as well as any need to perform simulations to obtain inflated Type-1 error.

OS 12.3

DIETARY GARLIC EXTRACT IN MODIFYING CLASTOGENIC EFFECTS OF INORGANIC ARSENIC IN MICE - TWO GENERATION STUDIES.

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Mice were fed by gavage daily crude garlic extract (100 mg / kg body wt.) for 30 consecutive days. One set was administered sodium arsenite (0.1 mg / kg body wt.) simultaneously. Another set was treated with sodium arsenite alone and mice given distilled water were kept as negative control. Exposed mice from each set were sacrificed and bone marrow preparations following standard air drying Giemsa schedule were examined for chromosomal aberrations and damaged cells. Sodium arsenite was a strong clastogen and the effects were reduced to a significant level by prolonged administration of garlic extract. For F_1 studies, exposed male mice were bred with exposed female mice and the progeny examined. In the progeny, clastogenic effects of sodium arsenite persisted, though in a lower degree, indicating that it is able to cross the transplacental barrier. There was no appreciable difference between the effects in progeny from parents given sodium arsenite alone and those given both the metallic salt and garlic extract.

OS 12.4

MODIFICATION OF CLASTOGENICITY OF COBALT BY DIETARY INGESTION OF *PHYLLANTHUS EMBLICA* FRUIT EXTRACT AS OBSERVED IN MOUSE BONE MARROW CELLS *IN VIVO*.

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Dried fruit of *Phyllanthus emblica*, a rich source of Vitamin C has been extensively used in Indian Ayurvedic medicine for a long time. The protective effect of

Phyllanthus emblica dried fruit extract was evaluated against clastogenicity induced by three different doses of cobaltous chloride on mouse bone marrow chromosomes *in vivo*. The parameter screened were percentage of chromosomal aberrations with and without gaps and percentage of damaged cells. Slides were prepared following the usual colchicine - hypotonic - fixative - flame drying - Giemsa staining schedule. Slides were screened after the expiry of 6, 12, 18, 24 hours. Statistical analyses indicated the protective efficacy of the extract than an equivalent amount of Vitamin C only when the two lower doses of the salt were used. The different stages of the cell cycle were affected.

OS 12.5

METHYLMERCURY DETOXICATION : A CHALLENGE

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Mercury and its various compounds are being used in a number of industries, agriculture and medicinal purposes. The multiple use of this heavy metal is slowly increasing its concentration in the environment and ultimately in the human beings. The methylated form of mercury is a potent neurotoxicant. A world wide hunt for mercury and methylmercury detoxicating agents is being carried out. More than 150 detoxicating agents have been tried by scientists throughout the world. Some of them have been found to be useful to eliminate mercury content from non- nervous tissues especially from liver and kidney. However, from central nervous system the metal is not mobilized . In the present study a model was developed using mice as an experimental animal. The animals were intoxicated with 1 mg/Kg MMC/day for a certain period and these pre- toxicated animals were treated with different doses of monothiols (glutathione and N-acetyl- DL- homocysteine thiolactone) and vitamins (B complex and E). The animal tissues were analysed for the mercury content, various essential elements and for enzymes of various metabolic cycles. The results verify that methylmercury can be removed from all the tissues, especially from central nervous system which is hitherto unknown till date.

OS 12.6

THE PROTECTIVE EFFECT OF PROPOLIS (BEE-GLUE) ON ISOLATED RAT HEPATOCYTES AGAINST HEPATOTOXICITY OF CARBON-TETRACHLORIDE.

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Propolis aqueous extract (PW-13) protects against carbon tetrachloride (CTC) hepatotoxicity in isolated rat- hepatocytes. Isolated rat hepatocytes were used as a model for CTC- hepatotoxicity (perfusion method). Preincubation of the isolated rat hepatocytes with a 13% aqueous propolis(Bee- Glue) extract (salomon propolis, Denmark) for 30 minutes at concentrations of 0.1 µl/ml, 1µl/ml, 10 µl/ml as well as 100 µl/ml exhibited

a protective effect on isolated rat hepatocytes against hepatotoxicity of CTC (at concentrations of 0.2 μ l/ml of CTC : DMSO, 1:1. v/v). The parameters measured included the assay for the depletion of glutathione, lipid peroxides as well as the release of the cytosolic lactate dehydrogenase. Aqueous propolis extract prevented the depletion of glutathione, the rise in lipid peroxides and the release of cytosolic lactate dehydrogenase induced by carbon tetrachloride.

OS 12.7

RELATIVE PROTECTION GIVEN BY CRUDE LEAF EXTRACT AND EQUIVALENT AMOUNTS OF CHLOROPHYLL AND CHLOROPHYLLIN AGAINST CYTOTOXIC EFFECTS OF CHROMIUM.

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Chromium oxide and potassium dichromate were compared with respect to their clastogenic effects and protection given by crude leaf extract of *Beta vulgaris* var. *Benghalensis* and equivalent amounts of chlorophyll extracted and chlorophyllin, following dietary administration for prolonged periods in mice *in vivo*. Chromosomes were observed from bone marrow preparations. The frequencies of chromosomal aberrations did not differ significantly between the two salts. The crude leaf extract and chlorophyllin reduced the frequency of chromosomal aberrations to a significant level but the chlorophyll extract was not effective. The protective action of the crude extract against the clastogenic effects of chromium, therefore, is the sum total of the interactions between the components of the complex crude mixture, rather than due to any single ingredient, like chlorophyll.

OS 12.8

THE PROTECTIVE EFFECT OF α - TOCOPHEROL AGAINST THE METABOLIC CHANGES INDUCED BY ENDOTOXEMIA.

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The effect of pretreatment with α - tocopherol on endotoxiosis was studied. Male Sprague Dawely rats were treated intraperitoneally (i.p.) with pyrogen free saline (P.F.F) or (100 mg/Kg b.wt.) α - tocopherol- (α - TOC). The rats were then given endotoxin (ETX) of *Salmonella typhimurium* in 2 doses, 24 hrs after the pretreatment and were sacrificed 24 hrs after ETX injection. The 2 doses of EXT used were: high dose (13 mg.Kg b.wt.) and low dose (2mg/ Kg b.wt.). In a similar group of rats not treated with ETX but given P.F.F., the effect of α - TOC (100 mg/ Kg b.wt.) alone was studied. A survival rate of 60% (12/20) was found 24 hrs after ETX (13 mg/Kg b.wt.) administration. Prior treatment with α - TOC (100 mg/Kg b.wt.) improved the survival rates of the affected rats to 100% (10 /10), 24 hrs after ETX administration. Serum

total cholesterol (T- Ch), triglycerides (TG), total lipids (TL), low desity lipoprotein cholesterol (LDL- Ch), very low desity lipoprotein cholesterol (VLDL- Ch), levels and the activities of glucose- 6 - phosphate dehydrogenase (G6PDH) in the liver, sorbitol dehydrogenase (SDH) and alanine aminotransferase (ALAT) in the serum were all significantly higher in rats treated with ETX (13 mg/ Kg b.wt.) than in the control rats. However in the same group of rats serum high desity lipoprotein cholesterol (HDL- Ch), albumin and glucose levels were significantly lower than in those of the control rats. Pretreatment with α - TOC (100 mg/Kg b.wt.) provided a complete protection against the changes in most of the parameters tested in the endotoxemic rats, except for serum SDH and ALAT activities which in spite of being alleviated by α - TOC pretreatment still remained above the control levels. Administration of 2mg/ Kg b.wt. ETX (sublethal dose) resulted in a significant increase in serum TG and glucose levels and SDH activity as compared with the control levels, but it had no effect on the rest of the parameters tested . Pretreatment with α - TOC protected against the increase in serum TG level and SDH activity but it had no effect on the hyperglycemia induced by sublethal dose of ETX. Rats treated with α - TOC alone had serum T- Ch TG, TL, LDL, Ch and VLDL- Ch levels lower than in the control rats, while the levels of the remained parameters were similar to those of the control animals. In conclusion α - TOC (vit, E) maximizes the survival rate and protects against the changes in lipids, lipoprotein cholesterol, albumin, glucose levels in the serum and G6PDH activity in the liver induced by ETX. However, it gives only a partial protection against the increase in serum SDH and ALAT activities .

Trends to Safer Alternatives

OS 13

PL 12

TRANSFORMATION OF ATMOSPHERE AND BIOSPHERE BY AGROCHEMICALS.

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Extensive work was directed in the last thirty years to study the transformation of atmosphere and biosphere as a result of extensive use of agrochemicals in Egypt. Egypt as an example for a country in third world, injected in the environment in the last 40 years 690450 metric tons of pesticides (182 different compounds) and 250000 metric tons of chemical fertilizers, while the whole world injected in the global environment 210.4 million metric tons of pesticides and 3024 million metric tons of nitrogen and 1503 million metric tons of phosphorous fertilizers. This work was directed to find answers for the following questions:- 1) Is the problem of environment pollution by agrochemicals in Egypt a local or international problem? ,2) What is the ancient Egyptian concept in soil and plant protections and why this concept is changed in the last 9000 years?, 3) How agrochemicals can be transported from local to global atmosphere?, 4) Can these agrochemicals and their breakdown products be transformed in the local and global atmosphere?, 5) What is the relation between

these chemicals and their breakdown products and the upersphere ? Can these metabolites and final products i.e. NO₂, SO₂, CO₂, P₂O₂, Cl, Fl ...etc play the same role of the chlorofluorocarbons? , 6) Can these agrochemicals be transported from Egypt to other parts of the world through atmosphere and rain water?, 7) Can these chemicals pollute the local and global hydrosphere? and how these chemicals find their way to the Mediterranean and red sea?, 9) What are the levels of these pollutants in Nile River, lakes, underground water, canalsetc? and what is their side effect on aquatic fauna?, 10) How these chemicals and their breakdown products find their way to the biomass ? ,11) How these chemicals concentrate in the living organisms?, 12) What are the side effects of the accumulation of these residues on plant cell, plant physiology, plant production?, 13) What are the side effects of these residues on soil microorganisms, macroorganisms, soil fauna and their activities (ammonia, nitrite and nitrogen fixation), and soil fertility?, 14) What are the side effects of these chemicals which were used extensively on the useful animals i.e., pollinators, honey bees, parasites and predacious insects ...etc?, 15) Can these pollutants accumulate in the trophic chains?, 16) What are the side effects of these pollutants on the Egyptian peoples in Rural and Urban areas?, 17) What is the relationship between the quantity of these chemicals used and the increased number of death cases by cancer, kidney and liver failure?, 18) Measurable amounts of agrochemical residues in our food and water present a variety of problems to the Egyptian people, what are the levels of these residues in our food stuffs and drinking water?. What is the total quantity of residues in the total diet samples?. What is the daily intake of these residues / person in Egypt? The lecture includes also answers to other important questions.

OS 13.1

SYNTHESIS OF SOME THIO-2,4 - DICHLOROPHENOXY ACETYL-AMINO ACIDS AND DIPEPTIDE ETHYL ESTERS WITH ANTICIPATED ANTIMICROBIAL ACTIVITY.

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Ethyl esters of 2,4- dichlorophenoxyacetyl amino acid and dipeptide could be thiated successfully with either lawesson's reagent (LR) or the Japanese reagent (JR) to afford the corresponding monothio and the dithio - analogues. The antimicrobial activity of the newly synthesized thiated compounds was assayed against some of the gram negative, gram positive bacteria and fungi. In general, the introduction of Sulfur enhanced the antimicrobial action. *Bacillus subtilis* NRRL B 543 was proved to be the more sensitive microorganism towards the tested thio - products. All the synthesized compounds were actually devoid of the activity towards the tested fungi *Aspergillus niger* NRRL 599.

OS 13.2

DEVELOPMENT OF BAIT FORMULATIONS FOR CONTROL OF INTERMEDIATE HOSTS OF AFRICAN SCHISTOSOME SPECIES.

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Exploration of methods of snail control indicated a need for a new control method since many failures in control programmes are due to lack of contact between molluscicides and the target snail population. One such approach to improve the molluscicide delivery is the development of bait formulations containing attractants and a molluscicide which would be ingested by the snails. This study was designed to prepare snail standard attractant pellets (SSAP) containing different molluscicides of plant origin, to remove target snails selectively with minimal adverse effects on the environment. In this study different sugars and amino acids were chosen for preparing SSAP. The reason for choosing both sugars and amino acids as attractant materials is their presence in both aquatic plants and decaying animals which constitute essential dietary requirement of the snails in the field. Moreover, snails use chemical sense as indicator for the presence of their food. Our previous results showed that starch was the most attractant compound for adult, juvenile and senscent *Biomphalaria alexandrina* snails.

OS 13.3

ISOLATION AND STRUCTURE DETERMINATION OF CHEMICAL CONSTITUENTS OF INSECTICIDAL LEGUME- *GLIRICIDIA SEPIUM*

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Gliricidia sepium (Jacq) Walp (Leguminosae) is a fast growing multipurpose legume and exhibits potential insecticidal activity against mosquito larvae. The larvae of different mosquito species showed difference in the mortality percentage depending on the dosage of ethanolic extracts of different parts of the legume. Subjection of the concentrated alcoholic extract of stem bark of *G. sepium* to silcion gel column chromatography and elution of the column with gradient increment of polarity furnished 32-hydroxyhexatriacont - 4- one, 21- methylhencont - 3 - on- 24 ol, 4-nonadecanone, heptacosan-3- en- 25- one, 16- hentriacontanone, dotriaconta-3- one - 26- 01, otacons- 10-en-1, 13- diol, hexacosane, a new diterpenic acid characterized as 3,7,11,15- tetramethylhexadeca -11-01-1-oic acid and a sterol dimer reported for the first time and identified as cholesta - 4-en-3-one-21- yl (cholesta-4'- en-3'- one-28-ol) - 21- ester. The structures of the isolated compounds have been elucidated by analysis of spectral data like UV, IR, ¹H NMR, EIMS, etc. and by chemical reactions.

OS 13.4

STRESS - INDUCED PHYSIOLOGICAL CHANGE IN INSECTS, ALTERNATIVE FOR PESTICIDES

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Stress induces release of neuroactive substances in insect blood. At sublethal doses, insecticidal phosphorus compounds caused increase of octopamine titers accompanied by CAMP level increase, trehalase activity suppression, and growth retardation in insects. Cold shock, heat stress, JH- esterase inhibitors, and JH I delayed pupation of *Tribolium Freemani* larvae. Cold shock and heat stress reduced JH- esterase activity. Cold shock and JH I reduced ecdysteroid level. Light, vibration, a nonsteroidal ecdysteroid agonist, and some octopamine agonists stimulated pupation. These facts indicate that some stress greatly affect insect growth and behavior and could be usable as alternative for pest control.

OS 13.5

TOXICITY EVALUATION OF *APODYTES DIMIDIATA* AS A POTENTIAL MOLLUSCICIDE AGAINST *BULINUS AFRICANUS* (PULMONATA) IN SOUTH AFRICA.

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Synthetic molluscicides have proved too expensive for third world communities for snail control in anti- schistosomiasis control programmes. An alternative which is not only cheaper, but also promotes self- reliance and empowerment in affected communities is the use of plants with molluscicidal properties. This study evaluates the toxicity of crude aqueous extracts of *Apodytes dimidiata* (E.Mey. ex. Arn.) leaves against the target organism (*Bulinus africanus*) and non - target organisms (earthworms, fish, rats and rabbits). These tests were carried out in accordance to the guidelines set down by WHO and OECO. Results clearly indicate that aqueous extracts of *A. dimidiata* are potentially useful for schistosomiasis control in South Africa and have proved non- hazardous to non- target organisms with the exception of low toxicity against fish. Consequently, field trials are now in the process of being implemented.

OS 13.6

BOTANICAL BIOCIDES. 1. TOXICITY OF SOME PLANT EXTRACTS TO MOSQUITO LARVAE AND MOSQUITOFISH IN LABORATORY.

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The preliminary screening for potency of 38 different extracts obtained from 19 plant species against *Culex pipiens* (L.) larvae, resulted in recommending 14 extracts of them for further toxicity evaluations on the insect and the predator mosquitofish, *Gambusia affinis* (Baird and Girard). The insect growth regulator Diflubenzuron was included in the bioassays as potent toxicant for comparison. Accordingly, the larvicidal potency of the selected extracts were grouped into: a) extracts more potent than Diflubenzuron (e.g. pet. ether extracts of *Piper nigrum*, *Melia azedarach*, *Artemisia judaica*, *Matricaria chamomilla*, *Cuminum cyminum* and *Cyperus rotunds*, as well as, the ethanolic extract of *P. nigrum*) ; b) extracts nearly potent as Diflubenzuron (e.g ethanolic extract of *Lupinus albus* and pet. ether extract of *Acacia nilotica*) ; and c) extracts less potent than Diflubenzuron (e.g. ethanolic extracts of *C. cyminum*, *M.chamomilla* and *Prunus aremiaca*, as well as, pet. ether extracts of *Allium sativum* and *Ambrosia maritima*). Most of these plant extracts, as well as Diflubenzuron, were found to be highly toxic to the fish as to the insect. But selective toxicity towards the insect without causing toxic risks to the fish, was exhibited by the extract of *L. albus*. The results obtained may encourage further investigations in this direction.

OS 13.7

BOTANICAL BIOCIDES. 2. PRELIMINARY SCREENING OF SOME PLANT EXTRACTS FOR MOLLUSCICIDAL, CERCARICIDAL AND MIRACICIDAL ACTIVITIES.

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Ethanolic extracts of 49 plant species representing 25 families were biologically screened for molluscicidal, cercaricidal and miracicidal activities. The results showed that 25 of the tested plant extracts gave ca. 100 % mortality to *Biomphalaria alexandrina* snails at a concentration of 1000 ppm (w/v). Moreover, 11 plant extracts showed 100% motality to miracidia when tested at 500 ppm in both cases. On the other hand, dry powders of the promising plants were used in the same concentrations (i.e. 1000 and 500 ppm). The results showed that the dry powder of 5 plants gave more than 50% mortality to snails, while the dry powder of 11 and 10 plants showed more than 50% mortality to cercaria and miracidia respectively. The results obtained would encourage further research in this important direction.

EGYPTOX SYMPOSIUM

Main Topic

Industry & Environment in Egypt

ES- 1

PL 13

COMBINED LONG-TERM EXPOSURE TO LEAD , MERCURY AND TNT IN EGYPT.

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In a trial to evaluate the clinical effects due to combined long term exposure to lead, mercury and TNT, 103 workers exposed to such materials in one of the military factories for explosives were studied. Their mean age were 46.5 ± 6.9 years and mean duration of exposure was 22 ± 6.4 years. The exposed and a control group (50) of the same age group and socioeconomic status, were subjected to complete occupational and medical histories, clinical examination, P-A chest X-ray, ventilatory function tests (F.V.C. and FEVI), ECG. as well as lead in the blood and 8-ALA in urine, liver functions & blood picture. Environmental analysis for the level of atmospheric Pb concentration in workplace is double ($280 \mu\text{g}/\text{m}^3$) the TWA level. The Pb-B level of exposed workers ranged between 30.2 to $74.6 \mu\text{g}\%$ (mean 43.14 ± 10.14) and for the nonexposed between 15 to $35.5 \mu\text{g}\%$ (mean 22.51 ± 7.19). There was significant rise in the serum levels of the enzymes studied (GPT, GOT, LDH and ALK.Ph) in comparison to their levels in the controls ($P < 0.001$). Albumin showed significant decrease ($P < 0.001$) among exposed workers and A/G ratio was significantly decreased as well liver functions were significantly affected among exposed workers with Pb- B up to $50 \mu\text{g}/\text{dl}$. It means that though Pb alone is hepatotoxic, yet the combined effect of it and TNT is more toxic. Through biological and experimental studies are recommended to assess and confirm the interrelation between lead, mercury and TNT.

ES- 1.1

ASSESSMENT OF SOME BIOCHEMICAL PARAMETERS IN WORKERS CHRONICALLY EXPOSED TO LEAD.

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The purpose of this study is to assess workers chronically exposed to lead as regards clinical manifestations and some biochemical blood and renal parameters. Fifty workers chronically exposed to lead were included. Venous blood and urine samples were tested to determine blood lead level, free erythrocyte protoporphyrin (FEP), serum urea, serum creatinine and serum uric acid, urinary (U) N- acetyl B-D glucosaminidase (NAG), U B₂- microglobulin (B₂-M), U Delta aminolevulinic acid (Delta ALA), and U total proteins. The mean blood lead level in exposed workers was $42.88 \pm 12.93 \mu\text{g}/\text{dl}$. The mean FEP, serum urea creatinine, uric acid, urinary ANG, UB₂ M, U Delta ALA, were significantly high in lead exposed workers. Blood lead level was positively correlated with FEP, U NAG, and U B₂ microglobulin. The use of non invasive, screening tests of urine e.g., urinary enzyme NAG, urinary B₂ microglobulin for detection of early renal dysfunction in lead exposed workers is recommended.

ES- 1.2

LEAD DEPOSITION ON A RESIDENTIAL AREA IN THE VICINITY OF LEAD SMELTER IN CAIRO CITY.

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This work is concerned with the role of the local source on the concentration of deposited lead at the surrounding residential area. Deposited dust was collected from 12 sites before and after closing the lead smelter. The collected samples were analysed for lead by atomic absorption spectrophotometer. The lead concentrations ranged from 0.015% to 1.2%, 0.07% to 0.16% before and after closing smelter respectively. Average Pb level in deposited dust collected before closing the smelter, was greater than that detected at other residential areas. Generally an inverse relationship of lead concentration with distance away from lead smelter is seen according to the wind direction. The concentration of atmospheric lead shows significant decrease. The percentage concentration of lead in total suspended particulate matter was 28%, 0.34% before and after closing the smelter. These results indicate that the lead smelter is the predominant source for lead pollution in this residential sector.

ES- 1.3

BLOOD LEAD LEVEL IN EGYPTIAN WORKERS

A.A. Shakour

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Lead has played a role in occupational diseases. The present study was done with the aim of comparing the pattern of blood lead level in workers exposed to lead in their work place in different industries, and to estimate the proportion of workers with blood lead that exceeds the normal limit of 40 $\mu\text{g}/\text{dl}$. Blood lead level (bll) was determined for 1943 workers. The (bll) = ranged from 116- $\mu\text{g}/\text{dl}$ to 11 $\mu\text{g}/\text{dl}$. However, about 59.65% of the investigated workers have (bll) exceeding 40 $\mu\text{g}/\text{dl}$. High values were found in the workers in the lead smelter (secondary smelter), meanwhile lower values were found in the workers in the soldering processes. The data show that there is a significant difference between the (bll) in the smoker and non- smoker workers in some industries ($p < 0.05$).

ES- 1.4

HEAVY METALS IN ATMOSPHERIC PARTICULATE IN THE INDUSTRIAL AREA NORTH CAIRO, EGYPT.

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Air pollution Dept. National Research Centre, Dokki, Cairo, Egypt

Particulate matter (suspended and dust fall) was collected for one year (Sep 1993- Aug 1994) from the atmosphere of an industrial area north Cairo City. Heavy metals were determined in the collected sampling using the atomic absorption spectrometry method. The obtained data

show that the particulate matter in this industrial area contained elevated concentration of Pb and Fe. The Pb concentration in the total suspended particulate ranged from 0.3-8.6 $\mu\text{g}/\text{m}^3$. This concentration exceeded much the international standard for lead. The rate of deposition for lead ranged from 78.4 to 79.3 g/m^2 day. This result showed that industrial emission is a major source of heavy metals in the area atmosphere.

ES- 1.5

TRACING OF SOME HEAVY METAL TOXICITY IN LAKE MANZALA ECOSYSTEM.

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As a complementary part of a toxicological study, the level of toxicity with zinc, lead, cadmium and mercury has been traced in three major components of Lake Manzala ecosystem namely; Lake water, fish and human urine samples. A total of one hundred samples were analyzed using PYE Unicomp Sp9 Atomic Absorption Spectroscopy and showed unacceptable toxic level according to the WHO 1982 standard. For instance, mercury estimates reached 5000 $\mu\text{g}/\text{L}$ in water, 280 $\mu\text{g}/\text{g}$ dry weight in freshly caught fish flesh and ranged from 7000-14000 $\mu\text{g}/\text{L}$ in urine samples. Tendency of cadmium to accumulate in fish flesh was recorded, 2.6 $\mu\text{g}/\text{g}$ dry weight. Eating of half kg of such a fish daily for a week will give an overall intake of 5250 μg while it should not exceed 500 μg /week according to the WHO 1989 reports. Urine samples analysis reflected clearly how high the concentration of these toxic metals in comparison with both the international standards and the control samples taken from volunteers away from the Lake population. The involvement of the studied metals are in the clinical disorders amongst the Lake ecosystem components was confirmed.

ES- 1.6

A COMPARATIVE STUDY BETWEEN IMPACT AND CONTINUOUS NOISE AS A STRESSOR FACTOR ON WORKER'S HEALTH

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Most reviews on noise and non-auditory health effects emphasize that noise is a potent stress and that the non-auditive effects spring from this fact. Our study deals with the effect of chronic noise stress on some biochemical parameters of the body among continuous noise-exposed workers , and impact noise -exposed workers. A control group of 30 administrators matched for age and sex with exposed groups was involved in this study. the results demonstrate high prevalence rates of different health impairment manifestations, higher levels of biochemical stress indicators (plasma cortisol, blood sugar) , also higher prevalence rates of ECG changes among noise exposed workers especially the impact noise exposed workers, compared with the control group. That is why impulse noise exposure conditions should be kept below the threshold level much lower than for continuous noise.

ES- 1.7

HUMAN POISONING CHOLINESTRASE INHIBITOR INSECTICIDES : CLINICAL AND LABORATORY STUDY.

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The aim of this work is to study patients with acute poisoning by cholinesterase inhibitor insecticides (ch EII) as regards clinical presentation, levels of serum pseudocholinesterase and amylase enzymes with evaluation of treatment. Fifty patients suffering from acute poisoning by chEII and admitted to ALEXANDRIA Poison Centre were assessed clinically and venous blood samples were withdrawn for estimation of serum cholinesterase and amylase levels. Inhibition of cholinesterase enzyme activity was observed in relation to severity of clinical manifestations. Elevation of serum amylase was observed. Clinical and laboratory investigations should be complementary to each others in diagnosis and treatment of patients with acute poisoning by chEII. A protocol for management was recommended.

ES- 2.1

LONG- TERM EFFECTS OF MANGANESE IN EGYPT.

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This study was conducted to evaluate the effects of exposure to different atmospheric concentrations of manganese in two different industries on clinical and certain biochemical parameters aiming to throw light on the dose response relationship for long- term exposure to Mn. Twenty four workers in a low alloy steel industry (group A) of mean age (45.2 years) and with mean duration of exposure to Mn (19.42 years), 47 workers in a dry battery industry (group B) of mean age (37.5) years with mean duration of exposure to Mn (16.07 years) and 20 non- exposed subjects of the age (mean) 32.1 years of the same socio- economic status and clinically free, were submitted to the study. Full history taking, clinical examination (including neurobehavioral), ventilatory function studies, electrocardiographic tracing (EKG), liver function tests and blood manganese levels, were done for the studied groups. 72.3% of group B, 33.3% of group A and 25% of the controls presented one or more of the neuropsychiatric symptoms. Also 61.7% of B and 25% of A and 10% of the controls have one or more the neuropsychiatric signs. These neuropsychiatric signs are mainly hypo-, hyper-reflexia, peripheral neuropathy, mask facies and tremors. The symptoms are headache, impotence, paraesthesia, anxiety, muscle weakness, tremors, dizziness, lassitude and : amnesia. Ventilatory dysfunction was 63.9%, 29% and 10% among group B workers, A and controls respectively. Liver dysfunction was more evident among group B albumin and A/G ratio was significantly decreased among both groups ($P < 0.005$), however, the total protein level was significantly decreased among workers of group B only ($P < 0.001$). Total globulins

and their simple fractions α_1 , α_2 , and γ showed significantly increased levels ($P < 0.001$) among exposed groups, while β - globulin was significantly decreased ($P < 0.001$) . Serum transaminases, alkaline phosphatase and lactate dehydrogenase activities were significantly elevated among both studied groups. We conclude that there is dose- response relationship in exposure to manganese, i.e. the higher the dose of Mn, the higher the percentage of those with clinical fundings especially neuropsychiatric symptoms and /or signs and liver function impairment.

ES- 2.2

POLLUTION ABATENENT EFFORTS IN SOME EGYPTIAN INDUSTRIES AFFILIATED TO MINING AND REFRACTORIES COMPANY.

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This paper deals with some of the pollution problems tackled and implemented in some Egyption companies affiliated to Mining and Refractories Company. The study concerns with cement, phosphate Fertilizers and ceramics and porcelain industries in Egypt. Our findings will be presented and discussed.

ES- 2.3

THE NEED TO INTEGRATED ENVIRONMENT PROTECTION LAW.

Sahar Hafez

National Center for Sociology and Criminological Research, Zamalek, Cario, Egypt.

Consequently it is necessary that the Government must take a precautionary approach to control of pollutants, relating to the scale of effort to the degree of risk. This basic principle will be conducted to be guided by a number of additional aims : to prevent pollution at source, to minimize the risk to human health and the environment, to encourage and apply the available technical solutions, while recognizing the integratd nature of the environment and the need to achieve the best practicable environmental options, to apply a critical loads approach by assessing the levels of pollutants that local environment can be tolerate and to ensure that the polluter must pay the restoration of the environment. These principles are unified in a new system of the integrated pollution control. The principle legislative weapon against the environment pollution must be "Integrated environment law" . Integrated environment control will be the best method for environment protection, accordingly it is necessary to change the concept of environmetal legislation to be integrated environment laws, puting in consideration that the source of environmental law is general laws, special laws, international laws and penal laws. The study proposed that fines may be applied to make the sanctions system more effective in addition to such measures as compansation of damages, confiscation and restoration.

ES- 2.4

HUMAN RIGHTS AND ENVIRONMENT

Sahar Hafez

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Health means more than an absence of disease. Health is only possible where resources are available to meet human needs and where the living and working environment is protected from life- threatening and health - threatening pollutants, pathogens and physical hazards. But health also includes a sense of well- being and security. Deficient living and working environment are associated with both physical and psychosocial health problems. This understanding of health also means, above all, that individuals, households and communities have substantial responsibility for their own health. Personal and community responsibilities for health are essential adjuncts to individual and community rights. The right of individuals to adequate shelter, health care and education (including environment education) must have as a counterpart their commitment to the promotion and protection of their own and their neighbours' health and welfare. Indeed, each adult has the duty as a citizen to ensure that health risks within human environments are minimized and government resources wisely used . Citizens' rights and citizens' capacity to organize and act become crucial in health.

WORKSHOP

Main Topics

- * Risk Assessment
- * Risk Management

W 1

THE ROLE OF RISK ASSESSMENT RISK MANAGEMENT AND RISK COMMUNICATION IN PREVENTING ENVIRONMENTAL POLLUTION-WITH PARTICULAR APPLICATION TO DEVELOPING COUNTRIES.

Yugal K. Luthra² and Donld F. Van Dyke³.

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As a part of the complimentary series of presentations, this portion of the workshop addresses salient features of the processes associated with risk assessment, risk management and risk communication. The objectives of the workshop are to discuss the concept of the basis of risk assessment, to evolve a common language of terminology in risk assessment, and engage in a dialogue to formulate a framework for developing risk- based managment decisions. Finally, we will consider how risk assessment and risk managment information as well as decisions may be communicated to the public. The workshop is not planned to provide a "cookbook" step- by - step approach to risk assessment but to explore both the science and other factors which influence risk assessment, risk management and risk communication. The participants in the workshop will focus on a hypothetical site- specific problem that may be encountered in a developing country on a day to day basis. Participants will be given the opportunity to evaluate quantatively a case study involving risk/ hazard posed to human health and ecology, and to recommend remedial measures to be taken at the contaminated site. Workshop participants will also practice "role play" in communicating the risk information to the public. Opinions expressed and information / data provided in the workshop are those of the authors only.

W 2

HAZARDOUS WASTE MANAGEMENT APPROPRIATE IN DEVELOPING COUNTRIES IDENTIFYING SOIL CONTAMINATION BY VISUAL INSPECTION, INTERNATIONAL REGISTRY OF CONTAMINATED SITES, ENVIRONMENTAL PROTECTION AN THE GOVERNMENTAL STRUCTURE OF DEVELOPING CONTRIES.

Donald F. Van Dyke¹, and Yugal K. Luthra².

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State of the art industerial technologies and practices, which are used in some developed countries , require less input materials , and generate less waste and

pollution. The result is lower cost over all , higher profits, and a cleaner environment. However, to obtain information about these technologies and management practices is difficult in developing countries. Furthermore, because many of the latest technologies have greater initial cost, some industries may be unable to redesign their facilities. Greater initial cost may also prevent newly constructed industries from utilizing "State of The Art" technologies. Thus , the environment in developing countries suffers, and industries in developing countries are at a disadvantage in global competition. This symposium will explore management practices and technologies suitable to some industries in developing countries. Group discussion will attempt to identify the obstacles and solutions for the incorporation of the newest technologies and management practices. The State of California is working to promote environmental technologies in Pacific-rim countries. This symposium will also explore the feasibility of directing these efforts to other developing countries. Pollution of air and water is increasingly capturing the attention of the citizenry in developing countries. However, soil pollution, because it is less obvious, is often overlooked. Contamination of soil is no less of a threat than air and water pollution. Runoff and leachate from contaminated soil pollutes both surface and ground water. Vapors and dust aggravate or induce illness. People who live or work near industrial sites may be chronically exposed. Soil sampling and analysis is needed to accurately identify soil contamination, however, other simple evidence frequently indicates the likelihood of contamination and the need for further testing. This symposium will explore the sources of soil contamination, discuss how to determine the likelihood of soil contamination through visual inspection, and consider the utility of an international registry of potentially contaminated sites based on visual inspection. Such a registry could be used to document the need for further testing and analysis , the need for remediation or cleanup technologies, and the need to require the pollution control technologies by both existing and newly constructed industrial facilities. Opinions to be presented in this symposium are solely those of the speakers and are not necessarily the opinions of the Department of Toxic Substance Control.

POSTER PRESENTATIONS

Main Topics

- * Biochemical Toxicology
- * Drug Toxicology
- * Metal Toxicology
- * Pesticide Toxicology
- * Toxicity Interaction & Complication
- * Preventive & Regulatory Toxicology
- * Monitoring Environmental Pollutants
- * Aquatic Toxicology
- * Natural Toxins
- * Genotoxicity & Neurotoxicity
- * Immunotoxicity & Carcinogenicity
- * Miscellaneous

P 1

PREVALENCE OF HEPATITIS B AND C INFECTIONS AMONG A GROUP OF LABORATORY TECHNICIANS.

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² Community Med. Dept., Fac. of Med., Mansoura Univ., Egypt.

The present study was designed to assess the prevalence of hepatitis B, and C virus infections among a group of hospital employees. The study population consisted of 81 female laboratory technicians working at Ain Shams University hospitals in Cairo, Egypt. A matched control group of 77 female clerks working at the same hospitals was used for comparison. The prevalence of anti-HBc positivity as an indicator for past or present HBV infection was 30.66%, with odds ratio 6.43 compared to controls. The prevalence of anti HCV positivity as an indicator for HCV infection was 37.03%, with odds ratio 3.94 compared to controls. Both markers were present in 17.26% of laboratory workers compared to 1.29% of clerks. Variables as age and duration of employment significantly affected the rate of anti- HBC and anti- HCV positivity among exposed group. The effect of risk factors as history of accidental needle sticks, history of blood transfusion, and duration of employment of 20+ years was also presented. Odds ratio of 5.40 ($P < 0.001$) 0.59 ($P > 0.05$), and 7.86 ($P < 0.001$) were obtained respectively. These data indicated that HBV and HCV infections are more common among laboratory technicians and mostly acquired from accidental needlesticks exposure during their professional lifetime. Liver function tests and ultrasonography revealed more abnormalities among exposed group which might be cautiously attributed to their hepatitis virus antibodies profile. Efficient precautions by which laboratory technicians regard all patients as potentially infected with a communicable blood borne agent are recommended.

P 2

EFFECT OF SUBLETHAL DOSES OF FENVALERATE ON CERTAIN BIOCHEMICAL PARAMETERS OF COTTON LEAF WORM AND MALE ALBINO RATS

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Fenvalerate, a pyrethroid insecticide, at two sublethal doses (LC_{10} , LC_{50}) induced certain biochemical alterations in the 5th instar larvae of the cotton leafworm, *Spodoptera Littoralis* under laboratory conditions. Levels of some enzymes and

electrolytes of rat kidney, liver and brain homogenates showed substantial disturbances after oral administration (2.7µg /g/hr) of fenvalerate for 7- 30 days. Larval contents of total lipids and proteins were significantly lowered while glucose, free amino acids and transaminases activity showed significant increase at both doses. Initial suppression of larval amylase activity at LC₁₀ and significant elevation at LC₅₀ were recorded, while other parameters remained relatively unaffected. Rat liver transaminases, kidney and brain ATPase activity were significantly increased after 15 and 30 days and even after 10 days of abstinence. Serum levels of Mg⁺⁺, Na⁺ and K⁺ were significantly elevated after 30 days, whereas Ca⁺⁺ showed no change. Fenvalerate virtually disrupted the major organ system while the duration of its administration potentially intensified its toxic effects.

P 3

BIOCHEMICAL ALTERATIONS INDUCED BY TWO INSECT GROWTH REGULATORS IN THE HOUSE FLY, MUSCA DOMESTICA (MUSCIDAE, DIPTERA).

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The comparative efficacies of two commercial insect growth regulators, Ataborn (IKI-7899) and sumilarv (sum- 71639), were studied, for economic considerations and better understanding of their action, via following some biochemical alterations in the house fly *M. Domestica* after feeding with different doses. Severe inhibition of protein synthesis in all insect stages was observed upon larval feeding with IKI and sumilarv. General reduction in lactic dehydrogenase, glycerophosphate dehydrogenase and acid phosphatase activity was observed in all stages evolved from larvae fed on IKI and sumilarv at all concentrations. The IKI proved to be more effective than Sumilarv even at relatively low doses.

P 4

ISOLATION AND CHARACTERIZATION OF N- ACETYLTRANSFERASE FROM SHEEP LUNG, LIVER AND KIDNEY.

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Middle East Tech. University, 06531, Ankara, Turkey.

Biological acetylation is one of the major conjugation reactions of animal species including humans. N - acetyltransferase (NAT) (E.C.2.3.1.5) is the enzyme which catalyzes the acetylation reactions. The enzyme was isolated from sheep liver, kidney and lung by differential centrifugation and the final cytosolic fraction was used as

enzyme sources. When stored at - 7°C, the enzyme activity was stable for at least 3 months in all tissues, however, at 37°C lung and liver enzyme was inactivated immediately whereas the activity of the enzyme was more stable, in kidney. Vmax and Km values were calculated from Lineweaver-Burk plots, and Vmax values were found as 5.9, 5.4 and 5.8 $\mu\text{moles/ml/min}$ and Km 26.3, 62.3 and 41.6 μM for kidney, lung and liver, respectively. For all tissues, a broad pH optimum curve was obtained ranging from 6.5 to 8.5. The inhibitory effects of certain ions and chemicals were also studied in order to compare the NAT activity in different tissues.

P 5

EFFECT OF FENVALERATE ON CIRCULATORY THYROID HORMONES AND CALCIUM STORES IN RAT BRAIN.

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Intraperitoneal administration of fenvalerate in male rats for 45 days in doses of 100 and 200 mg / kg body weight / day induced hyperexcitability, tremors and paralysis. Tremors were observed after seven days and gradually reached maxima on 45th day. The symptoms were more marked in rats treated with 200 mg / kg body weight / day. Fenvalerate provoked significant elevation of circulatory thyroid hormones, namely tri-iodothyronine and thyroxine. A significant increase in whole brain-and hypothalamic-total calcium and protein bound calcium was recorded. The elevation of circulatory thyroid hormones as well as the neurogenic active calcium pool were found to be dose dependent and the latter could be held responsible for tremorogenic activity. Tri-iodothyronine (T_3) and thyroxine (T_4) were estimated by Atomic Absorption Spectrophotometer.

P 6

EFFECT OF DIFFERENT METABOLIC INHIBITORS ON SOME BIOCHEMICAL PROCESSES WITHIN *BIOMPHALARIA ALEXANDRINA*

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The effect of different metabolic inhibitors namely: 4- amino- N-10-methyl pteroylglutamic acid "Methotrexate", 4- aminopteroylglutamic acid "Aminopterin", sodium arsenite, sodium arsenate and 2,4-dinitrophenol "2,4-DNP", on some biochemical processes within *Biomphalaria alexandrina* snails, were studied. Results showed that the nucleic acids DNA and RNA were more affected by folate antagonists (Methotrexate and Aminopterin), than by other inhibitors. Moreover, Methotrexate and aminopterin caused pronounced reduction in total protein content in snails, while sodium arsenite, sodium arsenate and 2,4- DNP had a slight effect on proteins. On the other hand, untreated and inhibitors-treated snails were subjected to infection with

miracidia of *Schistosoma mansoni*. Results revealed that the effect of folate antagonists was pronounced in minimizing the infection, while other inhibitors showed slight effect on the susceptibility of snails of infection by the parasite.

P 7

BIOCHEMICAL FINGERPRINTS OF THE COMMENSAL RODENTS IN EGYPT AND THEIR SUSCEPTIBILITY TO WARFARIN: 1- *RATTUS SPP*

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In order to detect and manage resistance effectively, basic data on the susceptibility of rodent populations is required for our country. The present study aimed at constructing biochemical baseline data concening the susceptibility of the normal populations of *Rattus spp.* to warfarin. Using the conventional feeding technique, results revealed that feeding animals a (50ppm) warfarin bait for 6 days for *Rattus norvegicus* or a (250 ppm) warfarin bait for 9 days for *Rattus rattus* is an efficient test for detection of resistance. In addition, the normal coagulability of animals was examined and distinct deviation would, therefore indicate the development of resistance. Moreover, when the electrophoretic patterns of the plasma proteins were compared, there have been significant differences between the two species. It is noteworthy that not only would the present study help in the identification of resistance but it would help identify the species, as well.

P 8

ON THE EFFECTS OF KHAT ON GUINEA PIGS

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³Pathology Dept., National Research Centre, Dokki, Cairo.

⁴Gynecologist & Obstrician, Sabeen Hospital Sanaa Yemen.

This work was conducted on thirty adult female guinea pigs, which were injected subcutaneously by Khat- extract for over 21 day. During the course of treatment, five animals died. On day 22, HCG plus vaginal stimulation were done to induce ovulation, and on day 23, the animals were sacrificed. All the test animals lost weight significantly. They also showed a significant increase in TSH, FSH, T₃ and T₄, while LH, serum prolactin, astrogen and progesterone showed a significant decrease. Histopathologically, the ovaries showed a decrease in the number of graffian follicles, which did not reach the preantral stage. Oocyte degeneration and stormal hyperplasia. The corpora lutea, which happened to form, showed insignificant pathological changes. The pituitary glands showed hyperplasia of acidophils and basophils at the expense of chromophobes. It happened that one animal was pregnant (excluded from

results), and its decidua showed an inflammatory reaction with foci of necrosis. This work shows that there is a detrimental effect of Khat consumption on oogenesis, steroidgenesis, and LH and prolactin secretion. The detrimental effect on the decidua suggests a further work on pregnancy- outcome and teratogenic effects of the plant.

P 9

A HISTOLOGICAL AND HISTOCHEMICAL STUDY ON THE EFFECT OF MORPHINE SULPHATE ON THE LIVER OF POSNATAL ALBINO RAT

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The effect of morphine sulphate on the induction of some histological and histochemical changes in the liver of newborn and young rats was studied. The animals at different ages (3,12,30 days) were injected daily with morphine sulphate (0.9 mg/Kg) for a duration time of 3 and 10 days. When compared with control, the liver structure of morphine treated animals showed some changes which were frequently dependent on the age and repeated dose parameters. The changes were represented by: (1) an increase of phagocytic sinusoid lining cell populations in the first week of life, (2) poorly stained vacuolated hepatocytes which were more prominent with the increase of age and time of morphine exposure, (3) the darkly stained connective tissue of blood vessels and reticulin fibers supporting hepatocytes and sinusoid lining cells, (4) the increase of both Golgi bodies and polysaccharide content in hepatocyte cytoplasm after 3 days of injection, while an obvious decrease was observed after 10 days of morphine treatment. These results suggest that morphine induces abnormal structural and functional changes in the liver during the postnatal development, and gives attention to further studies on the mechanisms of interactions between morphine exposure time, dose parameter and the age of developing animal.

P 10

MEASUREMENT OF SELECTED ENZYMATIC ACTIVITIES OF JUVENILE BIOMPHALARIA SNAILS IN RESPONSE OF EXPOSURE TO S.MANSONI INFECTION.

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Biomphalaria alexandrina snails, specific intermediate hosts for *S. mansoni* were subjected to selected enzymatic analysis at week intervals after exposure to parasitic infection. Aspartate and alanine aminotransferases, lactate dehydrogenase, and cholinesterase were measured. This investigation is an attempt to clarify metabolic integration during host parasite association. Measurement of these enzymes during the development of the parasite may give us a clue to understand the complexity and the diversity of host - parasite relationship. This study revealed that the most pronounced effect of the parasite on host's metabolism is within the 1st and 2nd weeks post

infection and that success of host - parasite association is mainly due to metabolic integration.

P 11

HEPATIC AND BODY WEIGHT EFFECTS OF KHAT ON ALBINO RATS

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Khat is an important item in social meetings in Arabian peninsula and African Horn Countries. It has some harmful effects but their documentation is scarce. The study was carried out on 24 albino rats, but 5 died on giving 10- time- dosage, one in the control and another in the 0.8 ml dose group. The body weight gain decreased with the increase of dosage. The liver histology changes, irrespective of dosage, in the form of vacuolation of hepatocytes with focal atrophy and necrosis, increased deposition of collagen around the central veins, hepatic sinusoids and portal tract, prominent Von-Kupffer cells with thickening of portal tracts were observed. ALT (SGPT) levels increased significantly in Khat treated animals and this increase was dose- related. A cause- result relation between Khat consumption and liver cirrhosis is suggested.

Drug Toxicology

P 12

COMPARATIVE CHROMATOGRAPHIC AND IMMUNOCHEMICAL FOLLOW UP OF MORPHINE IN URINE AFTER ADMINISTRATION OF - "OPIUM EXTRACT".

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Opium extract is a crude preparation of alkaloids obtained from opium and mainly used for illicit preparation of heroin. The present work deals with TLC, and GLC of this preparation. Comparative evaluation of chromatographic (TLC, GLC) vs. immunological (HI, RIA EMIT) methods in the follow up of morphine in urine from 4 patients who have abused this preparation was assessed.

P 13

**FORENSIC STUDY OF SOME HEROIN SEIZURES USING HPLC;
ASSESSMENT OF TOXIC ADULTERANTS.**

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For the clandestine produce of heroin from opium, the Lime method is the procedure most oftenly used. Crude heroin so prepared was found to contain other minor constituents of remarkable forensic value viz : monoacetyl morphine and acetylcodeine. Other minor constituents derived from opium are thebaine, naroctine. etc. The mixture is subject to many adulteration processes. Caffeine, strychnine, yohimbine and quinine are adulterants of choice in the black market of heroin. Extracting solvent : Acetonitrile- H₂O (50: 50 v/v) and 0.1% ammonium carbonate by wt. The latter was added to insure the presence of drugs as free bases. Filtration is necessary. If lactose, talc...etc are present. Replicates of 5µl injections of solution were made. The chart recorder provided an elution chromatogram of the mixture components. Caffeine, morphine, codeine, acetylmorphine, papaverine, heroin, yohimbin, acetylcodeine, narcotine, thebaine, strychnine, and quinine could be separated.

P 14

SHORT - TERM TOXICITY OF ALPHA- ASARONE IN RATS.

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Alpha - asarone, the major component of *Guatteria gaumeri* Greenman (Annonaceae), is an hypolipidemic agent in laboratory animals. Studies were undertaken to define the subchronic toxicologic profile of this compound, administered by oral route at doses of 5, 10 or 20 mg/Kg to groups of 15 rats of each sex, for 13 weeks. Another group administered corn oil served as negative control. Body weights, organ weights, haematology, clinical chemistry and histology were the criteria studied. Deaths occurred in two males at the highest dose which were directed attributable to effect of the compound. In this group there was also a decrease in weight gain (significantly in both males and females) which was associated with a marginal reduction in food consumption. Increased liver and kidney weights in these animals were considered to be related to treatment, but in view of a lack of histological abnormalities, this study did not demonstrate whether these were toxic effects. Decreased erythrocyte, hemoglobin, and platelet counts were also observed. Serum cholesterol was decreased

in all treated groups. It was concluded that the no-effect dose in this study was 10 mg/Kg/day.

P 15

TOXICITY DETERMINATION OF PLATIN COMPOUNDS UTILIZING TETRAZOLIUM AND NEUTRAL RED ASSAYS.

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The MTT (tetrazolium) and neutral red (NR) spectrophotometric assays were used to determine the cytotoxicity of two anticancer drugs, cisplatin and carboplatin, on murine erythroleukemic cells (GM-86) and the noncancerous Chinese Hamster Ovary cells (CHO). Following drug treatments, toxicity was assayed colorimetrically. In the MTT assay, tetrazolium was reduced to a dark blue formazan product which was assayed spectrophotometrically at 570 nm. The NR assay involved the colorimetric analysis of dye released from living cells at 540 nm. In both tests, the optical density is directly proportional to the number of viable cells. Overall, the data from both assays indicated that cisplatin was more toxic than carboplatin. Generally, dose- and time-dependent decreases in viability were exhibited by both cell lines. The leukemic GM-86 cells, however, proved to be more sensitive to both drugs, especially cisplatin, than CHO cells. The results obtained from both the MTT and the NR assays were comparable, indicating that both tests were equally sensitive and effective in identifying the toxicity of the two anticancer drugs.

P 16

IDENTIFICATION OF HIGHLY POLYMORPHIC S-MEPHENYTOIN HYDROXYLASE IN HUMANS.

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The metabolism of the anticonvulsant drug mephenytoin is highly polymorphic in oriented populations (about 20% of slow metabolizers) in comparison with caucasians, where reported that 4-hydroxylation of the S-enantiomer of mephenytoin is catalyzed by a cytochrome P450 enzyme from family 2C. There were a large number of efforts made to characterize this enzyme but its real identity remained unknown for many years. In this study S-mephenytoin hydroxylation activity was assayed in microsomes from genetically engineered yeast expressing P450s 2C8, 2C9 and 2C18. The activity was also assayed in a panel of human liver microsomes and the most extensively metabolizing microsomes were used for affinity purification of P450 proteins crossreacting with anti 2C10 antibodies. Preparations were electrophoresed

and blotted to nitrocellulose. Protein bands were subjected to protein sequencing via Edman Degradation. The amino acid sequence of a protein band whose intensity correlated with S- mephenytoin hydroxylation corresponded to the sequence of P450 2C19.

Metal Toxicology

P 17

CYTOTOXIC EFFECTS OF MERCURY SALTS ON PLANT SYSTEM IN VIVO.

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In Eastern India, Cytotoxic effects of mercurials are receiving importance due to increase in mercury levels in effluents of a chemical fertilizer factory in Meendweep Islands of Haldia, West Bengal. In the present investigation, the effects of inorganic mercury, as mercurous chloride, were observed on *Allium cepa* L. bulbs *in vivo*, following both short and long term exposure. The concentrations used ranged between 1 to 1000 ppm in aqueous solution. The endpoints screened were frequencies of cell division and chromosomal aberrations in root tip cells recorded following acetic ethanol fixation and aceto-orcein squash technique. Higher concentrations were lethal at higher durations of exposure. Both reduction in divisional frequency and enhancement of chromosomal aberrations were recorded with the lower concentration. Recovery in Knop's solution depended directly on the concentration used and duration of exposure.

P 18

COPPER INDUCED BIOCHEMICAL AND HAEMATOLOGICAL CHANGES IN *TILAPIA NILOTICA* FISH.

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The effect of exposure to sublethal concentration of copper sulfate for 3 weeks was studied in *Tilapia nilotica*. Marked elevations were recorded in the activities of serum glutamic pyruvic transaminase (GPT), glutamic oxalacetic transaminase (GOT), lactate dehydrogenase (LDH) and alkaline phosphatase (ALP). Serum total protein was increased with hyperglycaemia, while cholesterol concentration was reduced. Copper induced polycythemia was accompanied by increased haemoglobin (Hb) concentration, haematocrite (Hct) value and mean corpuscular haemoglobin concentration (MCHC).

In addition, leukopenia, lymphopenia and neutrophilia were observed. It was concluded that copper produces tissue damage, metabolic stress and malfunctions of the haematopoietic system in *T. nilotica*.

P 19

ALTERATION IN THE TOXICITY OF HEAVY METALS TO *SPIRULINA PLANTENSTIS* BY PH AND EDTA.

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The response of algae to heavy metals varies and decreases in the presence of chelators. The present paper discusses the toxicity of environmentally important heavy metals, Cu, Cd, Ni, and Cr on *Spirulina platensis*, a filamentous cyanobacterium, under different pH regimes, viz., 8.3, 7.2 and 6.4. The toxicity of the metals to the organism was studied by measuring dry weight biomass. At pH 6.4 the organism showed net reduction in biomass. During this period the pH of the medium increased. The highest toxic metal to *S. Platensis* was Cu and the least toxic was Cr. The toxicity of Cu and Cd was higher at pH 7.2 than at pH 8.3 or 6.4. Addition of EDTA to the culture medium reduced the toxicity significantly. The toxicity curve (EC50 vs. time) of these metals was asymptotic indicating an "incipient lethal level" of metals for the organism. Such studies can be useful in assessing pollution potential of toxic heavy metals in receiving water bodies and thus envisaging obatement strategies.

P 20

CARDIOVASCULAR EFFECT OF CHRONIC CADMIUM EXPOSURE IN RATS.

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Two groups of Sprague Dawley weaned 28 days old male and female rats were exposed to cadmium chloride in drinking water in a level of 0 and 25 mg/L, for 18 weeks followed by breeding of each group. Pregnant females of the exposed group were continuously exposed to cadmium during pregnancy and lactation. The first generation male offspring of the exposed group were continuously exposed to cadmium after weaning for 16 weeks, while male offsprings of the control group were maintained on zero level of cadmium in drinking water. Decrease in the body weight gain and increase in blood pressure and its responses to adrenaline, noradrenaline and isoprenaline were observed in the cadmium exposed males. However, blood pressure response to acetylcholine and histamine decreased in the same group as compared to the control. The heart rate of cadmium exposed rats decreased after administration of higher doses of adrenaline, noradrenaline and isoprenaline. Histamin in 60 µg/Kg led to

83% decrease in heart rate of 16% of the cadmium exposed rats compared with only 50% decrease in 11% of the control animals. A significant decrease in total cholesterol, triglycerides and HDL, and increase in LDL was estimated in the serum of cadmium exposed rats compared to the control.

P 21

CLASTOGENIC EFFECTS OF INORGANIC SELENIUM SALTS ON MICE BONE MARROW *IN VIVO*.

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Compounds of inorganic selenium are of continuing interest in toxicology in view of their protective action against other metals. Both anticlastogenic and antimutagenic activities have been reported. In the present investigation two salts of selenium administered *in vivo* to mice, however, induced both clastogenic and turbagenic effects. Five concentration each of sodium selenite and sodium selenate were dissolved in water (7, 14, 21, 28 and 35mg/ Kg body weight) and fed by gavaging to age and sex matched mice. Observations were made at intervals of 6, 12, 18 and 24 hours following the usual colchicine- fixative - air drying - Giemsa schedule. The endpoints screened were chromosomal aberrations and spindle disturbances. The frequencies of aberrations induced were directly proportional to the concentration of the chemical and within each concentration to the duration of exposure. Sodium selenite was found to be a more potent clastogen than sodium selenate.

P 22

CYTOTOXIC EFFECTS OF ARSENIC SALTS ON PLANT FOLLOWING CHRONIC EXPOSURE.

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Arsenic toxicity is assuming serious dimensions following severe contamination of drinking water (more than 0.3 mg/L) in several districts of West Bengal in Eastern India. The effects of sodium arsenite and sodium arsenate were compared on plant system *in vivo* using cytogenetic endpoints. The test system used was *Allium cepa* L. (Onion) and the salts were given in concentrations ranging from 1 to 10,000 ppm. Effects were screened from root- tips at intervals of 24 to 120 hours, following the usual pretreatment - fixation- acetoorcein squash schedule. The frequency of abnormal cells was directly proportional to the concentration of the chemical and inversely proportional to the duration of recovery. Mitostatic effects were also dose- dependent and decreased following recovery. Both clastogenic and turbagenic effects were recorded.

P 23

CHANGES IN THE REPRODUCTION OF INSECTS CAUSED BY DIFFERENT CHEMICAL COMPOUNDS

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Effects of selected chemical compounds - juvenoids, nucleoside derivatives- were studied in different insect species. In *Spodoptera littoralis*, *Spodoptera fugiperda*, *Mocis latipes*, *laspeyresia pomonella*, *pyrrhocoris apterus*, *Dysdercus cingulatus*, *Aphis fabae*, *pachneus lithus* and *Hylobius abietis* sterilizing effects were ascertained. Juvenoids and adenine nucleotide derivatives caused many pathological changes in ovaries - vacuolisation in ooplasm, pycnosis, disorganisation of nucleolus, inhibition of mitotic and meiotic division, degeneration and resorption of follicular and interfollicular epithelial cells and oocytes. These processes resulted in full or partial sterility. Sterilizing effects are accompanied with inhibition of vitellogenine synthesis. In nucleotide derivatives, some changes in genetic material were confirmed by *Drosophila* wing spot test. From this point of view, applications of these compounds without complete observation all of the effects would be harmful to many living organisms.

P 24

REDUCTION OF ENVIRONMENTAL POLLUTION BY USING A COMBINATION OF LAMBADA CYHALOTHRIN AND FOLIAR FERTILIZERS IN THE CONTROL OF TWO SUCKING INSECTS IN TESTING COTTON FIELD:

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The present study is an attempt to study the efficiency of combined treatment of Lambada - cyhalothrin (EMA- 27831), and foliar fertilizers against the cotton whitefly *Bemisia tabaci* and cotton aphid *Aphis gossypii* compared with Lambada- cyhalothrin applied alone, at three different rates of applications (twice the recommended rate, recommended rate and ½ recommended one). The interaction between nutrient (Complezal or Multimicro - E) and the insecticide was evident and differed widely in their response to the two cotton varieties tested (Giza 75& 81). The foliar fertilizers applied, either alone or in combination with Lambada - cyhalothrin, were able to protect the two varieties of cotton plants against mature and immature stages of cotton whitefly in the field trials. Although the candidate fertilizers did not change the initial insecticidal activity in their mixtures, they had a significant role in increasing the

residual activity of Lambada - cyhalothrin; where the efficiency of the recommended rate of Lambda- cyhalothrin alone was equal to the half recommended rate + foliar fertilizers.

P 25

NEMA-TOXICITY OF SOME SYSTEMIC NEMATOCIDES IN RELATION TO NEMATODE MODE OF PARASITISM IN VITRO.

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The objective of this study was to evaluate nematicidal activity for some systemic nematicides against three plant parasitic nematode genera of different mode of parasitism, i.e., endo, semi - endo, and exoparasitic. Second stage larvae of the endoparasitic nematode, *Meloidogyne incognita*; the semi - endo - parasitic nematode, *Tylenchulus semipenetrans*; and stages (O + O + Iv.) of the exo- parasitic nematode *Helicotylenchus spp.* were tested as 500's in Syracuse dishes. Nematodes were extracted from specific naturally infested fields in Giza Governorate(Embaba country). Mortality was recorded 24 hrs after nematicide application. In vitro test for nematotoxic - contact - action, expressed as LC_{50} , revealed the positive correlation between nematode mode of parasitism and concentration of the tested nematicides. The endoparasitic nematode larvae, *M. incognita* proved to be the most susceptible. The semi-endo parasitic nematode larvae, *T. semipenetrans* proved to be moderately susceptible. The ecto- parasitic nematode, *Helicotylenchus spp.*, proved to be the least susceptible. These results were identical in all the tested systemics at different concentrations used. Tested nematicidal activity, expressed as ppm, were in a descending order as follows: Aldicarb, Phenamiphos, Oxamyl and Carbofuran.

P 26

GENOTOXIC EFFECT OF AN ORGANOPHOSPHOROUS PESTICIDE

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The increasing use of pesticides was reported to be genotoxic. The organophosphorous pesticide malathion not only induces damage to the chromosome but also reduces the frequency of division. The *Allium* root tip cells exposed to malathion, when post- treated with *Phyllanthus* extract and distilled water could neither restore the normal mitotic index nor bring about reduction in the mitotic irregularities. However, the residual analysis of the treated and post- treated cells showed the absence of pesticidal residues.

P 27

TOXICOLOGICAL STUDIES CONCERNING THE EFFECT OF PURE AND FORMULATED PARATHION ON PROTEIN CONTENT AND NUCLEIC ACIDS SYSTEM IN ALBINO RATS.

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Parathion in pure and formulated forms at a sub - lethal dose of 1/20 LD₅₀ was orally administered or dermally applied every two days for three months in order to determine the synergistic toxicity on RNA and DNA, protein, RNase and DNase in different organs of the adult male albino rat. The contents of RNA, DNA and soluble protein as well as DNase and RNase activities were determined in liver, brain and kidney. The results showed that pure and formulated parathion, either orally or dermally introduced, resulted in an increase in RNA and soluble protein contents. However, the DNA content was not affected as compared to control. On the other side, the activity of DNase and RNase was stimulated under the same conditions of application. The formulated parathion was found to be more effective than the pure one and the oral route was more effective than the dermal one, as well. That is to say that the order of effectiveness was as follow : formulated parathion (oral) > pure parathion (oral) > formulated parathion (dermal) > pure parathion (dermal).

P 28

VITAMIN K REQUIREMENTS OF THE WARFARIN SUSCEPTIBLE STRAIN OF THE NORWAY RAT (*RATTUS NORVEGICUS*) IN EGYPT.

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²Plant protection Dept., Fac of Agric., (Fayoum), Cairo, Univ. Fayoum, Egypt.

The reported high susceptibility of warfarin resistant Norway rats to vitamin K deficiency directed our interest towards the fact that, in order to detect and manage resistance effectively, the nutritional requirements of the susceptible strain should be established. Albino and brown rats were fed vitamin K- free diet for 10 days and then given a single i.p. dose (0.36 mg/kg) of vitamin K. The coagulation index as well as the electrophoretic pattern of the plasma were checked at 0, 4, 7, 10 and 11 days from the beginning of the experiment. The results revealed that rats fed a vitamin K- free diet showed obvious hypoprothrombinaemia, confirmed in the brown rat. A parallel decline in the activity of vitamin K- dependent factors was observed. On the other hand, a plasma protein band (R_f= 0.41) completely disappeared in the case of the brown rat. However, 24 h after the injection of vitamin K₁, the albino rat almost recovered but the injected dose was not capable of curing the induced coagulopathy in the brown rat.

P 29

TOXIC EFFECT OF DIMETHOATE ON THE COLLAGEN METABOLISM IN FEMALE ALBINO RATS.

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The toxic effect of dimethoate on the collagen metabolism was studied in female albino rats. In dimethoate treated animals, the synthesis of collagen and rate of catabolism of both soluble and insoluble collagen were found to be decreased. The urinary output of both glu-gal-hyl and gal-hyl was also appreciably lower from dimethoate treated animals. Among the mechanical properties, the tensile strength was found to be decreased in skin and tendon. The thermal behaviours, namely, shrinkage temperature isometric tension and the temperature at the isometric tension were also decreased in both skin and tendon due to the effect of dimethoate. The results indicate that due to the effect of dimethoate, collagen metabolism and crosslinks are impaired.

P 30

COMPARATIVE TOXIC EFFECT OF PROMETRYNE AND ATRAZINE HERBICIDES AND THEIR BIOACCUMULATION IN *BIOMPHALARIA ALEXANDRINA* SNAILS.

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Biomphalaria alexandrina snails are the intermediate hosts for the parasite *Schistosoma mansoni* which causes the hazardous disease schistosomiasis. Thus, control of this disease may be achieved through the eradication of these snails by certain molluscicides or compounds that are toxic to these snails either by killing them or by affecting their normal biochemical composition, and hence the parasite life cycle may be interrupted. The toxic effects of prometryne and atrazine herbicides which are normally employed in the fields were studied on *B. alexandrina* snails. The LC₅₀ of the two herbicides after 72 hr. was investigated using gas liquid chromatography. The results showed that the LC₅₀ of prometryne was 20 ppm while that of atrazine was 250 ppm. On the other hand, the uptake and bioaccumulation of both herbicides by snails were found to be 3.2 ppm (3.2 µg/gm) and 14.3 ppm, (14.3µg/gm) respectively. Also the residual content of the two herbicides in the incubation water was 8.6 ppm. and 130.6 ppm, respectively. Based on this toxic effect of herbicides, they may be used as molluscicides and, thus serve as double function against snails and against herbs, thus reducing the addition of extra pollutants to the water.

P 31

COMPARATIVE STUDIES ON CERTAIN NITROGENOUS METABOLITES IN DIFFERENT DEVELOPMENTAL STAGES OF FRESH WATER SNAILS HOSTS AND NON- HOSTS TO SCHISTOSOMA PARASITE.

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Citruline and Nitric oxide in relation to nitric oxide synthetase were measured in Juvenile, premature, mature and old - aged *Biomphalaria alexandrina* and *Bulinus truncatus* molluscan intermediate hosts to Schistosoma parasite. Parallel investigations were done on *Lymnea truncatula* and *Physa acuta* as non host species for Schistosoma parasite. The effect of exposure to parasitic infection on the measured parameters was elucidated. Moreover, the effect of nitric oxide synthetase inhibitors on the rate of cercarial shedding was studied.

P 32

THE EFFECTS OF MALATHION ON DWARF LIZARDS (LACERTA PARVA, BOULENGER 1887).

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Lizards (*Lacerta parva*, Boulenger 1887) were exposed to oral doses of malathion (1, 2 and 3 mg/Kg) for 16 weeks. Possible toxicological effects on body weight, life span, tail regeneration and histopathology of liver, kidney and small intestine were investigated. Body weights, the length of regenerated tails and life span of lizards in groups given malathion were found to be significantly lower than lizards in control group. Mostly, the highest dose of malathion caused histopathological changes in liver, intestine, kidney and small intestine. General characteristics of the effects of malathion on tissues were fatty degeneration, mononuclear cell infiltration, hepatocellular necrosis in liver, paranchymal and vacuolar degeneration in tubules of kidney, atrophic changes in duodenum mucosa and hypersecretion of goblet cells in small intestine.

P 33

RESIDUES OF PIRIMIPHOS- METHYL ON STORED POTATO- TUBERS

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Potato- tubers were treated with the recommended rates of pirimiphos- methyl under the normal conditions of storage in perforated carton boxes for different intervals of time. The effect of washing and peeling processes was studied. A high percentage of the insecticide residues was removed in the washing process. Analysis revealed that the insecticide residues were concentrated in the peels and very little amounts penetrated into the pulp which were below the maximum limits for pesticide residues level. Desethyl pirimiphos-methyl, 2-diethylamino-6-methyl-4-hydroxy pyrimidine, 2-ethylamino -6-methyl-4- hydroxy pyrimidine, and 2-amino-6-methyl-4-hydroxy pyrimidine were detectable as the degradation products of the insecticide in stored potato tubers after 12 weeks.

P 34

DEGRADATION OF MALATHION IN WATER SPEEDED BY CATIONIC SURFACTANTS.

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A potentially important application of cationic surfactants is in decontamination because many toxic pesticides react with nucleophilic anions. Cationic surfactants assist degradation of these materials by solubilisation and speeding reaction with anion reagents. Laboratory studies concerning hydrolysis of malathion in water using a cationic surfactant are presented. Chemical degradation of samples containing malathion in distilled water using different concentrations of Cetyl dimethyl benzyl ammonium chloride (CDAC) surfactant is evaluated using gas chromatography. Efficiency of malathion degradation process reached 99.98% after 11 days using 15 mM CDAC.

Toxicity Interaction & Complication

P 35

SOME BIOCHEMICAL STUDIES ON THE ASPARTIC ACID- FRUCTOSE INTERACTION PRODUCTS (MRP'S).

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several biochemical parameters were carried out in the sera and liver tissue of experimental animals to assess the effect of the aspartic acid- fructose (AF) interaction products (MRP'S) on their biological functions. Fifty female albino rats of mean weight 110 ± 10 gm were assorted in five equal groups according to the following scheme : Group I : fed the normal diet and used as control, Group II : received orally 0.1 LD_{50} volatile AF 120 daily for 90 days, Group III : received orally 0.25 LD_{50} volatile AF 120 daily for 90 days, Group IV : Fed 5% nonvolatile

AF 120 mixed diet for 90 days, Group V : Fed 10% noneolatile AF 120 mixed diet for 90 days. Serum glucose and urea nitrogen levels, as well as liver glycogen content showed significant elevations in groups II and III, due to enhanced gluconeogenesis. The same parameters were also found to be significantly decreased in groups IV and V due to malnutrition as a result of bad palatability of the diet. Serum total cholesterol, triglycerides level and liver total lipids content were significantly reduced in all the tested groups. Serum total protein, albumin, globulins and liver total protein were significantly elevated in group IV and V (amounted to 14.2 and 37% respectively) compared to normal controls. Serum and liver levels of alanine transferase (ALT), aspartate transferase (AST) and alkaline phosphatase (ALP) were markedly elevated in all group. However, non- significant alterations in serum creatinine and total bilirubin levels were observed, compared to normal controls. Results obtained, pointed out to the commutative effect of Millard Reaction products (MRR'S) of AF 120 in vivo. Although these compounds were found to possess a significant biological effect, yet they are considered physiologically toxic on long term feeding in case of accumulation. Thus, there is a great possibility that during food processing under high browning conditions (120°C), some toxic compounds could be produced.

P 36

COMBINED EFFECTS OF ENDOSULFAN, DIMETHOATE AND CARBARYL ON MALE RATS.

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Endosulfan (E), dimethoate (D) and carbaryl (C) are widely used pesticides against cotton pests in Mediterranean regions of Türkiye. In this experiment, the combine effects of these three pesticides on male albino rats were investigated morphologically, hematologically and biochemically. 0.612 mg/Kg of endosulfan, 2.04 mg/Kg of dimethoate and 1.01 mg/Kg of carbaryl were chosen for dosing. Three and two dose combinations of pesticides (EDC, ED, EC and DC) were given orally to rats for 3.5 months. None of the pesticide combinations caused any statistically important change in body weights rats. Spleen and liver weights of rats in DC group showed significant decrease while liver weights of rats in EC group increased. Number of monocytes of rats in ED group and number of eosinophilic leucocytes of rats in EC group increased significantly. All doses of the pesticide combinations caused apparent decrease in the number and % of basophilic leucocytes. In addition, blood urea nitrogen (BUN), creatinine, cholesterol and total bilirubin levels also decreased.

P 37

EFFECT OF SELENIUM- MERCURY INTERACTION ON *CLARIAS LAZERA* FISH.

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Fish meat is an important source of protein for pollution. Since fish may absorb dissolved trace elements and heavy metals from food and surrounding water, these metals may accumulate in various tissues with significant amounts. Among these metals, mercury is one of the most hazardous to fish and human beings due to its binding to sulphhydryl groups. Toxicity and interactions of different elements are well-known. One of them is the antagonistic behaviour of mercury and selenium. Most studies revealed that presence of selenium reduces the toxicity of mercury in fish. This interaction known to be concentration - dependent. Our studies were performed to estimate the suitable concentration of selenium required to reduce the residual amount of mercury in fish muscle, the tissue of greatest concern to humans. *Clarias Lazera* fish were exposed to high and low levels of mercury in the absence and presence of high and low levels of selenium. Our results revealed that selenium reduces the residual amount of mercury in fish muscle, that was exposed to high level of mercury and low selenium level. Therefore, lakes and channels known to be polluted with high level of mercury could be treated with selenium to lower the residual amount of mercury in fish muscle.

P 38

EFFECT OF MONO- SODIUM GLUTAMATE ON NEW BORN RATS BY TWO ROUTES OF ADMINISTRATION.

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One of the commonest substances used for flavouring purpose is glutamic acid and its salt, mono - sodium glutamate. The latter is used very broadly in most commercially prepared frozen food containing meat or fish and in all dry soup stocks. It was being added to baby foods in pureed vegetables to enhance their flavour. Glutamic acid, being an amino acid present naturally in many foods and human body, has been regarded as harmless. Recent studies suggested that there may be unpleasant effects when large amounts are ingested. Various countries regulate the use of mono - sodium glutamate as a food additive. Some international reports excluded the use of mono - sodium glutamate by humans under the age of 12 weeks. The aim of our study is to study the effect of mono - sodium glutamate in new born rats by ingestion and injection routes. In the meantime the level of plasma glutamate in both groups was determined. Our results showed no evidence of damage and sterility in the group received mono-sodium glutamate by oral route. In contrast significant brain damage and sterility were shown in the injected group.

P 39

PESTICIDES AND *DAPHNIA* .5. TOXICITY INTERACTION OF INSECTICIDE MIXTURES TO *CERIODAPHNIA QUADRANGULA*.

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Two methods were used to analyze the joint action of paired insecticide mixtures to *Ceriodaphnia quadrangula*. In a single- dosage tests carried out with 45 mixtures, 32

combined pairs were found to produce potentiation effects, while 6 pairs caused additive effects and other 7 pairs induced antagonistic effects. In a multi- dosage tests, a simple formula was proposed to analyze the joint action of insecticide mixtures. According to the results obtained, the former method may be used as a first tier in the course of screening mixture for toxicity, generally, while the latter method, which depends upon establishing regression lines for the mixtures tested, may be used as a second tier whenever confirmation of results and / or more accuracy are needed.

Preventive & Regulatory Toxicology

P 40

ON EXPERIMENTAL STUDY OF SOME POSSIBLE MECHANISMS OF ANTICARCINOGENIC ACTION OF ORIGINAL PEPTIDE DUODENINE

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It has been previously reported that duodenine (D) - original peptide isolated from pig's intestinal tissues inhibits the carcinogenesis induced with some N- nitrosamines, benzo (a) pyrene (BP), urethane by 30- 75%. However, the data on the possible mechanisms of anticarcinogenic action of D are insufficient. The studies are now underway to determine the effect of D on some early damages of cell genome, induced by BP. The results of our study showed that D (50 or 500 mg/kg by gastric intubations 3 times a week for 20 days) reduced chromosomal aberrations frequency in mice bone marrow induced by BP (25 mg/kg by intraperitoneal injections daily for 5 days). Sperm- shape abnormalities assay did not show statistically significant changes in experimental groups. The study is being continued using other doses and treatment regimen for tested compounds in those test- systems.

P 41

DIETARY SUPPLEMENTATION WITH *EMBLICA OFFICINALIS* FRUIT EXTRACT IN REDUCING CYTOTOXIC EFFECTS OF LEAD-SUBACETATE.

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Aqueous extract of fruit of *Embllica officinalis* (685 mg/kg b.w.) was administered by gavaging on alternate days to laboratory bred Swiss albino mice, *Mus musculus* for 30 days. The mice were injected intra- peritoneally lead- subacetate- a known carcinogen (200 mg/kg b.w.) in aqueous suspension, three times a week for the duration of the experiment. Controls were maintained in distilled water. Both lead salt and crude

extract were administered singly as control. Bone marrow preparations were made following colchicine – fixativ air dry – giemsa schedule. Slides were scored blinded for chromosomal aberrations. Lead subacetate given alone was strongly clastogenic (CA 19.3%). Priming of the mice with the fruit extract reduced significantly the clastogenic effects of the lead salt, though not to the level of the fruit extract.

P 42

STUDY OF THE PROTECTIVE EFFECT OF DEFERROXAMINE ON CADMIUM INDUCED LUNGS AND HEART TOXICITY IN RATS.

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In this study we examined the possible protective action of deferroxamine as a chelating agent on cadmium- induced lungs and heart toxicity in albino rats. Six groups of rats were used in this study. The 1st group (5 rats) was used as a control group. The 2nd group (10 rats) was given 1mg/kg/day cadmium chloride intraperitoneal (I.P) for three days. The 3rd group (10 rats) was given the same dose of cadmium chloride in conjunction with 50 mg/kg/day deferroxamine I.P for three days. The 4th group (10 rats) was given the same dose of cadmium chloride for three days, but in the first day only it was given a single dose of deferroxamine (50 mg/kg). The 5th group (10 rats) was given 50 mg/kg/day deferroxamine (I.P) for three days. The 6th group (10 rats) was given a single dose of deferroxamine for one day. The animals were sacrificed 24 hr after the last dose. The heart and lungs were examined histologically. The histological findings in the heart and lungs in the second group were most profound. The third group showed focal areas of partial recovery. The data suggest that specific dose of deferroxamine is able to reduce the cadmium- induced lung and heart toxicity in rats.

P 43

SOME POSSIBLE RISK FACTORS IN ALLERGIC CONDITIONS AMONG CHILDREN BELOW 11 YEARS.

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In an attempt to study the different environmental factors which can increase the risk of sensitization in a genetically predisposed individual, and in order to determine if changes in the environmental and early diagnosis were able to favour prevention of allergic diseases, 216 children aged < 11 years were diagnosed. Results showed that 46.3% have bronchial asthma, 25.9% allergic rhinitis, 20.8% atopic dermatitis and 6.9% allergic conjunctivitis. 40.3% Of the patients were suffering from more than one allergic disease. 100 Cases of healthy controls matched for age, sex and socioeconomic standard were included. Positive family history of atopic disease was present in (69.4%) of patients, compared to (12%) of the control. Seasonal variations showed

increased allergic symptoms during late autumn, winter and spring. Exposure to adverse indoor environmental conditions were studied and revealed a significantly higher percentage of most of these conditions among patients than controls. Correlation between these conditions and different allergic diseases were done. For dietary history, food related symptoms were present in 27.8% of patients, 75% of them had a positive history of early weaning. Leucocytosis was present in 37%, lymphocytosis in 51% and eosinophilia in 78.7% of patients. Detection of antibody levels showed that serum Ig E level was high in all patients with the highest value in patients suffering both bronchial asthma and atopic dermatitis. The results of this study revealed important recommendations for prevention of allergic diseases.

Monitoring Environmental Pollutants

P 44

HAIR AS A BIOINDICATOR FOR THE DAILY INTAKE OF LEAD BY EGYPTIAN PEOPLE.

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Two hundred and thirty four samples of Egyptian hair from both adult and children (less than 15 years old) were analyzed for lead. Samples were collected from four locations (Moshtohor village, High polluted area in Cairo (Ramsis and Tahrir Squares). semi polluted area (El- Maadi) and an area nearly free from pollution (El-Salhia). The daily intake of the Egyptian people of lead through respiration is varied greatly according to rural or urban areas and according to the density of traffics and the numbers of factors. While the daily intake of each person in the highly polluted area in Cairo through respiration is 0.034 mg/person, it is 0.007, 0.003 and 0.0001 in El-Maadi and El-Salhia. The daily intake of the Egyptian person from water is 1.316 mg/person where the Egyptian person drink 2.810 litre/day. The daily intake of lead through meal diet was estimated to be 0.592 mg/person. That means that the daily intake of Egyptian person from lead varied between 2.891 and 2.246 mg/ person. Results indicated a marked variation of the hair- Pb concentrations which were detected in the different samples from the four localities. The mean level of lead which was detected in adult hair was 95.3 ppm. at highly polluted area, while it was 59.3, 35.7 and 23.7 ppm in El- Maadi, Moshtohor, Salhia respectively. While the levels were 83.3, 52.0, 31.0 and 11.4 for children in the same tested areas respectively. Results indicated that there is a correlation between the daily intake and the level of lead in Egyptian hair. While the correlation between air pollution and the level of lead in hair was very clear.

P 45

THE RELATION BETWEEN THE DAILY INTAKE OF HEAVY METALS AND THEIR LEVELS IN THE EGYPTIANS TEETH.

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it is well known that 94 - 95 % of the total body lead (body burden) is accumulated in bones. Teeth have been used in this study as indicator of integrated long - term exposure and have the advantage that samples are easy to procure. One hundred and thirty five samples of teeth were collected from rural (Moshtohor village) and urban (Shobra El- Khema) areas. The daily intake of the Egyptian people lead through respiration, drinking water and through meal diet was estimated for the people in both areas. Data indicate that the daily intake of lead through respiration for the adult was 0.003 and 0.02 mg/person in both Moshtohor and Shobra El- Khema respectively. While the daily intake of lead through drinking water for both was 1.316 mg/person. The daily intake of lead through meal diet was estimated to be 0.592 mg/person. Results indicate that the mean daily intake of the Egyptian person from lead varied between 1.928 mg/ person in Shobra El- Khema and 1.911 ppm/ person in Moshtohor village. The level of lead, varied greatly in the teeth of persons in both tested areas. While the mean level of lead in adult persons was 55.52 ppm in Shobra El- Khema, it was 28.72 ppm in Moshtohor. For that the level of lead in human teeth can be considered as bioindicator for their daily intake.

P 46

IMPACT OF AIR POLLUTION ON HUMAN LUNGS AND EYES.

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The deteriorating environmental conditions are leading to a variety of ailments in human population. Increasing vehicular traffic in urban localities is one of the major source of pollution faced by developing countries including India. We have simultaneously assessed the levels of suspended particulate matters (SPM), sulphur dioxide (SO₂) and nitrogen oxides (NO_x) along with the clinical survey of directly exposed subjects. Preliminary investigations conducted on a total of five hundred reveal that 48.2% taxi drivers and 55.4% vendors (operating near taxi stands) had complaints related to eyes and lungs. Majority of (52.4 %) exposed cases were suffering from the burning of eyes, watering in eyes (11.1 %), haziness in vision (9.2 %), redness (4.0 %), pain (4.0%) and irritation (3.3 %). The investigation in lung related ailments showed the prevalence of cough (18.4%), sore throat (4.8%) feeling of heaviness (3.7%) and occasional breathlessness (11.0 %). A correlation was found

to exist between the environmental status and the problems of eyes and lungs in the exposed population.

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OCCURANCE OF ORGNOCHLORINE PESTICIDES IN FRESH WATER FISH IN ASSIUT MARKETS.

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Organochlorine pesticides: total DDT complex (p,p' - DDT, o,p'- DDT, p,p'- DDT and p,p' - DDD); hexachlorocyclohexane isomers (alpha-, beta-, gamma- and delta-isomers); heptachlor and heptachlor epoxide; aldrin and dieldrin; endrin and hexachlorobenzene (HCB) were investigated in five species of fresh water fish (*Oreochromis niloticus*; *Clarias lazera*; *Labeo niloticus*; *Bagarus bayad* and *Synodontis species*) collected from Assiut markets. Chlorinated residues were analyzed by gas chromatography with electron capture detector (GS- ECD) using capillary column. The analytical results revealed that all samples were contaminated with one or more of the investigated pesticides. Total DDT complex, total HCH isomers were found in all analyzed samples with the highest values, followed by indrin, HCB, dieldrin, and heptachlors. Total DDT complex averages were 1.077, 1.865, 3.911 and 3.476 ppm, while total HCH isomers averages were 0.297, 0.160, 0.108, 0.093 and 0.029 ppm in the investigated five species, respectively. The residue levels detected were compared to those of the international limits and its hazardous effects were discussed.

P 48

RECOMEND TWO PLANT BIOASSAYS FOR TOXICOLOGY STUDY.

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Tradescantia (#03) micronucleus bioassay and *tradescantia* (#4430) stamen hair mutation bioassay are efficient tests for genotoxicity of environmental pollutants. Since 1980 , they were universally and successfully used in China and were validated and recommended by International Program on Chemical Safety , WHO & UN in 1991. The two bioassays are effective , simple and economical , so it would be particularly applicable in Developing Countries. Large population of *tradescantia* #03 and #4430 have been vegetatively propagated in the field of institute . We developed a practical packing technique to maintain plant living during duration of long distance shipping. So we could serve as a supply house of these plant materials to all corners of the world.

P 49

LEAD, IRON, COPPER, ZINC, MANGANESE AND CADMIUM LEVELS IN SOME FOODSTUFFS OF ANIMAL ORIGIN: CHEESE AND LUNCHEON.

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Seventy chees and fifty luncheon samples were randomly collected from Assiut city markets representing the most kind consumed in Egypt including hard, processed and soft (imported and local) chees and luncheon products of two companies (represented by A and B) over a period of ten months from January to October 1994. Samlpes were analysed for estimation of lead , iron, copper, zinc, manganese and cadmium levels by atomic absorption spectrophotometer. The obtained results revealed that lead , iron , copper, zinc, manganese and cadmium mean values in different kinds of chees were 0.28 ± 0.01 , 26.24 ± 1.7 , 2.9 ± 0.1 , 20.2 ± 4.7 , 2.4 ± 0.1 and 2.9 ± 0.2 mg/ Kg dry weight , respectively. Kareish chees was found to contain the highest values of lead , copper, manganese and cadmium with an averages of 0.55 ± 0.03 , 5.2 ± 0.8 , 4.5 ± 0.4 and 5.4 ± 0.4 mg /Kg, respectively. Damietta chees contained the highest levels of iorn with a mean level of 32.7 ± 5.4 mg /Kg dry weight, while the highest values of zinc was found in local hard cheese with a mean level of 43.6 ± 20.3 mg /Kg dry weight . 100 % of cheese samples contained lead values higher than 0.10 mg /Kg dry weight . Relatively higher values of estimated elements recorded in local cheeses in comparison with imported types. The mean values and the total mean of these elements in luncheon of the two companies (A and B) were , 0.93 ± 0.15 , 1.15 ± 0.17 and 1.03 ± 0.11 for lead ; 71.9 ± 12.07 , 76.8 ± 11.2 and 73.1 ± 8.05 for iron ; 12.9 ± 3.87 ; 13.9 ± 3.03 and 12.9 ± 2.38 for copper ; 60.6 ± 8.84 ; 61.3 ± 7.8 and 61.0 ± 5.8 for zinc ; 5.3 ± 1.4 ; 7.25 ± 1.5 and 6.27 ± 1.05 for manganese and 5.08 ± 1.56 ; 5.3 ± 1.32 and 5.13 ± 0.99 mg /Kg for cadmium . 59% of the total samples contain more than 0.5 mg lead /Kg ; 58.5 % of samples contained zinc values higher than 56 mg/Kg and 55% contained higher levels than 0.9 mg cadmium /Kg. Possible health risk of these elements was also discussed.

Aquatic Toxicology

P 50

INFLUENCE OF TEMPERATURE ON THE VARIATION IN THE TOTAL LENGTH OF DAPHNIA MAGNA NEONATES.

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Daphnia magna is the cladoceran species most frequently used as test organism in aquatic toxicology studies. *D. magna* neonates (organisms less than 24-h old) are the preferred development stage, as they are more sensitive in their toxic response. In this study, the standard and the total length (in μm) was measured in random samples of neonates produced

in successive clutches, in controlled cultures. Experiments began with two sets of 40 *D. magna* parthenogenetic neonates, individually distributed in 120-ml glass flasks containing 100 ml of reconstituted hard water. Two temperatures were applied: 20 and 25 °C. The green microalga *Ankistrodesmus falcatus*, in concentration of 400,000 cell ml⁻¹ was supplied as food. The replicates were daily reviewed and the offspring, when observed, was separated off the mothers. A random sample of at least 50 neonates per each clutch was measured at the microscope; this procedure was followed for all the consecutive clutches produced during 40 days. A two - way ANOVA indicated that both, temperature and the number of the clutch, had a significant effect on the neonate average total length, with the first two broods being the shortest recorded in both temperatures (<1250 µm). The mean size from the 3rd to the 13th clutch ranges from 1300 to 1480 µm; the neonates produced at 20 °C were frequently longer than those observed at 25°C. Differences in size could influence the sensitivity of the neonates to toxic compounds.

P 51

PESTICIDES AND *DAPHNIA*. 6. A PRELIMINARY STUDY ON THE USE OF *DAPHNIA* HEART BEAT AS A CRITERION FOR QUALITATIVE BIOASSAY OF PESTICIDES IN WATER.

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The effect of sub-lethal concentrations (e.g. EC₅₀, 1/2 EC₅₀ and 1/10 EC₅₀) of different insecticides, representing organophosphates (OP), carbamates (C), and synthetic pyrethroids (PY), on *Daphnia* (e.g. *Ceriodaphnia quadrangula* or *Daphnia magna*) heart beat rate was found to vary depending upon the chemical structure and concentration of the tested insecticides. For example (OP) compounds increased the heart beat rate at EC₅₀ level only, while (PY) compounds decreased it at 1/10 EC₅₀ only. The other concentration levels of both insecticide groups, as well as carbamate insecticides (C) at any level of the tested concentrations, induced no changes in the heart beat rate. This led us to propose a method for quantitative bioassay of pesticides in water using *Daphnia* heart beat as a criterion of estimation. The method is posed as a preliminary study regarding to its application for qualitative assay purposes, but the results obtained provide some basic information which may help to understand the mode of action of certain insecticides to daphnids.

P 52

TOXIC EFFECT OF DBSS ON LIPASE ACTIVITY OF *MOINA MACROCOPA*

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The detection of biochemical response to pollutants and the mechanisms of toxic action have received considerable attention in the assessment of stress effects in contaminated ecosystem. In this work, the effect of sodium dodecylbenzenesulphonate (DBSS) on lipase activity of *Moina macrocopa*, was studied. This detergent is an important contaminant of different water

bodies in Mexico. In homogenized *Moina macrocopa*, DBSS was added in order to give different concentrations of DBSS (e.g. 0.25 permissible concentration, 2.5, 25 and 250 mg / l). The homogenate was maintained at 25°C for 30 min. incubation period, thereafter lipase activity was measured. The results showed that DBSS permissible concentration in the water bodies must be revised.

P 53

TOXIC EFFECT OF DBSS, PB AND OIL ON MEMBRANES OF MOINA MACROCOPA.

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The modification of the lipoperoxidation grade (LI - Pox), lipids and reduced glutathione (GSH) concentration of exposed organism appears to be of value in the assessment of contaminants toxicity. The change of three biochemical parameters have been associated with damage of the membranes integrity. Some of Sodium dodecylbenzenesulphonate (DBSS), Pb and oil (OP) are important contaminants of different water bodies in Mexico. In this work, the effect of the three pollutants on membranes of *Moina macrocopa* was studied. To homogenized cladocerans, different concentrations of DBSS, Pb and OP were added. The cladocerans were incubated at 25°C for 30 min. GSH concentrations and LIPOX grade were determined. The results showed that the lipids and GSH decreased and Lipox was augmented. As a conclusion, we suggest using of these biochemical parameters as early warnings to evaluate the health conditions of an ecosystem.

P 54

CHROMIUM (Cr) INDUCED CHANGES IN THE OVARIAN ACTIVITY OF SKIPPER FROG RANA CYANOPHLYCTIS (SCHN.)

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The present study deals with the impact of chromium (Cr) on the ovarian activity of *R.cyanophlyctis*. As the intermediate trophic member of the food chain, this species plays a vital role in the control of pest population and hence needs careful preservation of its habitat free from pollution. The gonosomatic index (GSI), percent changes in different stages of oocytes and histology of the ovary of untreated frogs were found to be normal. The combined exposure to Cr (5.8 and 17.4mg/l) and temperature (15 and 35°C) resulted slight decrease in the GSI values as compared to control and no ticeable change in the recovery of GSI was observed after the Cr treatment was withdrawn. Treatment of frogs with both concentrations of Cr resulted reduction in FGP number and slight increase in other stages. Cr at low temperatures (15°C) inducated slight increase in number of some stages of oocytes while at high temperature (35°C) it showed a reverse effect. In Cr injected (100 and 200 ug/Kg body wt) groups there was a slight decrease in FGP number while other stages like MSGP, LSGP and AF showed enhancement in their number. Deformities of oocytes and their shape,

vacuolation, degeneration of germinal vesicles, fibrosis of cytoplasm and increasing atretic follicles of all stages of oocytes were some of the more pronounced histological changes noticed during Cr exposure periods.

P 55

ACUTE TOXICITY OF HEXAVALENT CHROMIUM TO *DAPHNIA MAGNA* NEONATES OBTAINED UNDER DIFFERENT CULTURE CONDITIONS.

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Daphnia magna is a freshwater microcrustacean widely used as test organism in aquatic toxicology bioassays, and recently a test method with this species was developed and incorporated in the Mexican environmental legislation. In order to estimate the sensitivity of test organisms from consecutive cultches produced under different culture conditions, in this study we assessed the acute toxicity (48 hours) of Potassium Dichromate (as hexavalent chromium), with *D. Magna* neonates obtained up to the 15th clutch, in cultures carried out at either 20 or 25°C, with photoperiod of 16 : 8 or 14 : 10 (light : dark), during 40 days. Despite of the origin, toxicity tests were conducted at 20 and 25°C, both at a photoperiod of 14:10. LC₅₀'s were estimated though the semilog and the probit methods, determining that neonates from the first and the last clutches (during the observed period), were significantly more sensitive to the toxicant. Origin of neonates did not produce a significant effect ($P > 0.05$) on the toxic response of test organisms, whereas the clutch in which they were produced (directly related with the mother age), had a significant effect ($P < 0.009$) only for the tests carried out at 20°C. Comparatively for the same brood number, the determined LC₅₀ was lower for the neonates exposed to the toxicant at 25°C. The average LC₅₀ values were 0.2076 ± 0.0164 and 0.1544 ± 0.0175 mg l⁻¹, respectively at 20 and 25°C.

P 56

EFFECT OF VOLUME CULTURE AND FEMALE CULTURE DENSITY, ON THE PRODUCTION OF *DAPHNIA MAGNA* NEONATES.

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The freshwater cladoceran *Daphnia magna* has a wide distribution in the Holartic region where frequently dominates the limnetic planktonic community, playing a very important role in the trophic relationships. This daphnid has many advantages as test organism, and nowadays is considered as an international reference species in toxicological studies. Nevertheless, some problems have been detected with respect to the toxicological response of the neonates. Variation in sensitivity is often related with the culture conditions (food type and concentration, female age, temperature, water quality, etc). In this study we assessed the effect of female density and volume of culture for neonate production. Densities from 5 to 40 org. l⁻¹, in volumes ranging from 100 to 400ml, were tested. Nine treatments were applied, each with

10 replicates. The green microalga *Scenedesmus incrassatulus* was applied as food (1.3 ± 0.6 cell ml^{-1}). Experiments were conducted during 40 days, assessing every day the survivals and the neonates produced (these were immediately separated from the mother in order to avoid additional effects in density). The maximal total progeny per individual was achieved in the density of 5 ind. l^{-1} in 200 ml culture volume, following the treatment of 10 ind. l^{-1} in a volume of 100ml. Even though the fecundity was reduced as we increase the density and the volume of the culture, the produced total progeny was higher and it could be an advantage in the management of the culture.

P 57

REDUCTION OF TOXIC HEAVY METALS IN *EICHHRONIA CRASSIPES* (WATER HYACINTH) TO BE USED AS FODDER CELLULOSE.

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In Egypt, *Eichhronia crassipes* is found in large quantities in the River Nile. This presents several problems such as pollution and consumption of the Nile water. Conventional methods for getting rid of this part by herbicides cause more pollution. Therefore it was necessary to remove this plant mechanically. The chemical analysis of *Eichhronia* showed that 60% hollocellulose, 20% lignin, 30% hemicellulose also and it contains 1.6% nitrogen. However, the analysis of *Eichhronia Crassipes* showed that it contains several heavy metals such as lead, copper, iron, and cadmium at levels higher than the threshold as safe material that may cause health hazards. Since that this plant can be used as fodder cellulose, these heavy metals content must be reduced. The experiments conducted in this work aimed to decrease heavy metals content in the plant to make it suitable as fodder cellulose. The reduction occurred by extraction with certain concentration of HCL. In addition, the nitrogen content was increased by treatments with nitrogenous compounds in order to increase its value as fodder cellulose.

P 58

BACTERIOLOGICAL CHARACTERISTICS OF ISMAILIA CITY SWIMMING POOLS.

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As a part of water surveillance at Ismailia City, all the swimming pools were surveyed during summer 1994, in order to check compliance with the recommended residual free chlorine (2-3 mg/L) and (pH range 7-7.6). Staphylococci, streptococci and aeromonads found in the pools water, in relation to the (RFC), water depth, surface area and age of swimmers were studied. Out of the nine studied pools only two were found within the recommended national (RFC) levels. Commensal bacterial counts expressed in total viable bacteria (TVB) as cfu/ml were found directly responding to the (RFC) while the other studied bacterial genera were not. Unlike pools used only for children or only for adults, pools used for both had the highest bacterial counts; TVB reached 444 cfu/ml, staphylococci 100/100 ml, streptococci 106/100 ml and aeromonads 78.6/100 ml. Generally TVB counts ranged from 155 to 914.25 cfu/ml, staphylococci counts ranged from 3 to 105/100 ml, streptococci counts ranged from 7 to 203/100 ml and aeromonads counts ranged from 1.33 to 152.66/100 ml. Whatever the reasons these counts are unacceptable according to the international standards for swimming pools.

Natural Toxins

P 59

REPRODUCTIVITY OF FEMALE RABBITS FED ON DETOXIFIED AFLATOXIN CONTAMINATED RATION BY HIGH PRESSURE AMMONIATION.

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An investigation was conducted to study the effect on reproductivity and blood metabolites in female pregnant rabbits of detoxified aflatoxin contaminated ration using 4% ammonia autoclaved under high pressure (HP) at high temperature. Two experiments were performed using 5 groups of rabbits. In experiment 1, rabbits at early pregnancy (E) were assigned to 3 groups, the first control group (EC) fed on control diet, the second group (E/HPI) that received a detoxified ration immediately after ammoniation and the third group that fed on a detoxified ration 90 days after ammoniation process (E/HP2). Rabbits at mid pregnancy were divided into 2 groups in experiment 2, a control group (MC) that fed on a control diet and a treated one (M/HP) that fed the detoxified ration. Pregnancy failed to be completed due to foetal resorption in rabbits of (E/HP1), (E/HP2), and (M/HP) groups. All experimental rabbits in (E/HP1) group died during 30 days, while in (E/HP2) group, only half of the treated rabbits survived. The survived rabbits in (E/HP2) group succeeded to concept and became pregnant 75 days after feeding on the detoxified ration. In (M/HP) group, the treated rabbits which were kept on decontaminated diet could be conceived after 45 days and completed pregnancy with normal parturition. The variations in plasma levels of progesterone, cortisol, enzymes and metabolites were recorded.

P 60

EFFECT OF GAMMA IRRADIATION ON AFLATOXIN PRODUCTION BY *ASPERGILLUS PARASITICUS*.

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Exposure of aflatoxins produced by *A.parasiticus* grown on sterile raw peanuts to specific gammas irradiation doses induced reduction in aflatoxins with increasing gamma irradiation dose than did aflatoxin from non- irradiated sterile raw peanuts (control). The reduction of aflatoxins ranged from 9.3 to 29.7% ; 13.9 to 37.3% ; 0.96 to 16.8% and 0.72 to 60.3% for AFB₁, AFB₂, AFG₂, when the culture was irradiated at 0.5 to 5 KGY respectively. On the other hand, non- sterile raw peanuts that was inoculated with conidia of the fungus and then incubated for two weeks at 30°C following irradiation resulted in reduction in aflatoxins ranged from 18.2 to 89% ; 26 to 96% ; 35.4 to 85.2% and 17.3 to 76.4% for AFB₁, AFB₂, AFG₁ and AFG₂ respectively. Irradiated raw peanuts culture following inoculation with conidia of the fungus and then incubated for two weeks at 30°C resulted in reduction of toxin(S) production ranged from 4.9 to 28.4% ; 16.8 to 54.7% ; 1.71 to 18.6% and from 9.13

to 30.4% in AFB₁, AFB₂, AFG₁ and AFG₂ when cultures irradiated at 0.5 to 5 KGY respectively. Inoculation of either sterile or non- sterile raw peanuts cultures following irradiation resulted in completely degradation of aflatoxin (s) at higher doses between 2.5 to 5 KGY for sterile substrates and at 2.5 to 4 KGY for non- sterile raw pea

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STUDIES ON PREGNANCY FAILURE IN RABBITS DUE TO AFLATOXICOSIS.

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NewZealand pregnant rabbits were used to test the pathological effects of aflatoxins on reproductive performance and blood metabolites as well as histopathological changes during early and mid pregnancy. Rabbits were randomly assigned to treatment groups fed experimental diets containing 4 mg aflatoxins/ kg ration at early pregnancy (E) for 4 weeks and mid pregnancy (M) for 2 weeks. In trial 1, experimental animals were divided into a control group (EC) that fed aflatoxin free ration, and an aflatoxin group (EA) fed on aflatoxin contaminated diet, immediately after conception. In trial 2, rabbits were assigned to control group (MC) and a treated group that fed on aflatoxin diet two weeks after conception (MA). Criteria of pregnancy and mortality rate were recorded, and blood samples were obtained for determination of glucose, cholesterol, total protein and fractions, ALT, AST, urea and creatinine, as well as progesterone and cortisol hormones. At the end of the trials, rabbits were sacrificed for postmortem examination, and specimens from each animal were taken for histopathological studies. All rabbits in (EA) and (MA) groups failed to complete pregnancy and pathological examination of ovaries and uteri revealed occurrence of corpora lutea and resorption of foeti. Liver shrinkage, kidney enlargement and severe hemorrhages on lungs and intestine were noticed in aflatoxin fed rabbits which died after 30 – 60 days. Levels of progesterone and cortisol hormones as well as blood enzymes and metabolites showed significant variations.

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GENOTOXICITY OF OCHRATOXIN AND ITS EFFECT ON GROWTH AND YIELD OF *VICIA FABA*.

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The genotoxic effects of different seed soaking treatments of ochratoxin A have been studied in *Vicia faba*. The applied treatments induced reduction of mitotic activity and inhibition of DNA and RNA synthesis in root cells. The toxin treatments also produced a variety of chromosomal abnormalities, represented by stickiness, disturbance, laggards, breaks, bridges and micronuclei. The genotoxicity of ochratoxin is also manifested as alterations in the

electrophoretic seed protein banding profile. In addition, the effect of ochratoxin on germination, plant growth and yield of *Vicia faba* was also studied. Significant reductions in criteria were scored. A correlation between the different effects of the toxin is evident.

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TOXICITY STUDIES ON CYNANCUM ACUTUM L. LEAVES IN ALBINO RATS.

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Cynancum acutum L., (Asclepidaceae) is a wild plant grown in Egypt and used for healing mouth ulcer in Folk medicine. The intraperitoneal (I.P.) LD₅₀, doses in rats were : 5.87- 4.2 g/Kg.b.wt. for total alcoholic and crude alkaloid extracts, respectively. The toxic symptoms in both extracts were loss of appetite, increasing respiratory rate, abdominal convulsion, then general paralysis and death. Sub - acute toxicity was performed, using 6 groups of rats weighing 100±5 g.b.w. The first two groups were fed a diet containing 10, 20% dried leaves of *C. acutum* and the 3 rd was kept as a control. Meanwhile, the 4th & 5th groups were I.P. injected with 1/5 & 1/10 LD₅₀ of crude alkaloid extract, the 6th was injected with saline. 45 days post- daily treatment, blood samples and specimens of different organs were collected for haematological and histopathological examinations. Anaemia was observed in 20% fed group, and in the two injected groups with crude alkaloid extract. Also, leucopenia and lymphocytopenia were obtained in such groups. Moreover, there was no major abnormal histopathological changes in the examined tissues. Only, mild reaction in different organs (kidney, lung, spleen, ovary and testes) occurred. While, the 1/5 LD₅₀ of crude alkaloid extract caused degenerative changes in the liver tissues of the treated rats. The present study concluded that *C. acutum* L. is more safe than other members of the same family. It has minimal harmful effects on different tissues even at higher doses. So it can be used safely in patent medical preparations.

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EFFECT OF VICINE AND DIVICINE ON GLUTATHION, HAEMOLYSIS AND MORTALITIES IN DIFFERENT SEX AND AGE IN ALBINO RATS.

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Vicine (V) is a glycoside found in *Vicia faba* beans, and by acid hydrolysis divicine (DV) is produced. V and DV were shown to cause favism. Favism is a metabolic disorder in which glucose - 6 - phosphate dehydrogenase (G6PD) and Glutathione (GSH) are deficient. Favism like signs appear upon ingestion of faba bean which may lead to a haemolytic crisis. In this investigation, *in vivo* experiments were conducted to study the effects of V and DV single lethal doses of 400 and 25 mg/100 g.b.w., respectively on Sprague - Dawley rats. V and DV were administered intraperitoneally (IP) in rats of different sex and age. Animals were divided

into 3 groups (1,6 & 24 months old) of 12 rats each in addition to a parallel age control group. GSH level, RBC haemolysis and mortality rate were determined in all groups. One hour following injection, the GSH level severely declined (about 50% than control values) in young and elder males of both sexes (1 & 24 months old). However, the adults were also affected by V and DV but not as the previous groups. Generally, DV caused hemolytic effect more than V- treated animals. V and DV caused 100% mortalities among 1 month old rats within 48hr., while DV- adult and elder groups (6 & 24 months old) died within 72hr. The mortality rate in V-treated rats was increased significantly in males than females. The survival% was increased in adult than in elder animals (males : 17% - 12% & females : 25- 17%) by V injection. It could be concluded that , DV is more toxic than V. Favism like signs occurred more strongly in male – than female rats and in young more than elder ones.

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ACUTE TOXICITY OF WATER EXTRACT OF *PRUNUS AFRICANA* IN RATS.

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Prunus africana (Hook.F) syn. *Pygeum africanum* Rosaceae has useful medicinal properties. Chloroform extract is used to treat human benign prostatic hyperplasia. Aqueous extract is used in folklore treatment of bovine babesiosis in Kenya. Acute toxicity of lyophilized aqueous extract (10% w/v) was determined in Sprague - Dawley rats (8/dose). A single intraperitoneal dose was administered per group from selected logarithmically spaced doses (based on a previous trial). Controls received the vehicle. LD50 was 0.85g/Kg body weight. Lethal doses caused death within 24 hours. Sublethal doses (down to 1.25g/kg) caused moderate or no clinical signs. Death was preceded by signs of accelerated breathing, hind leg weakness and prostration. Postmortem revealed extreme congestion of Peyer's patches, lymph nodes and spleen. Lymphocytolysis and lymphoid depopulation in lymph nodes, thymus, Peyer's patches, spleen and bone marrow were the major microscopic lesions. Other lesions were haemorrhages in the heart and myocardial degeneration. Lymphocytolytic effects of this extract may considerably influence the immune system in animals.

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ISOLATION AND IDENTIFICATION OF MYCOTOXINS PRODUCED BY *FUSARIUM SPP*, AND *ALTERNARIA SOLANI*.

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Fusarium oxysporum f.sp. *lycopersici*, *Fusarium solani* and *Alternaria solani* were isolated from tomato and pepper seeds and diseased plants. *Fusarium Spp.* and *Alternaria solani* grown on artificial media produced toxic substances which increased in concentration with the age of culture. These toxic substances inhibited growth of radicles or (hypocotyl, cotyledonary leaf and plumules) when seeds were germinated in the filtrate of the fungus. Inhibitory effect of extract appeared to be due primarily to phytotoxicity. Studies were extended to test the

biological activity of fungal toxins. Toxins produced by *Fusarium spp.* and *Alternaria solani*, at different temperatures, pHs, carbon and nitrogen sources, inhibited growth of *Bacillus megaterium* and *Bacillus mycoides* which differed in its toxicity to bacterial growth. *Fusarium spp.* secreted zearalenone and trichothecenes in liquid media. Maximum amounts of zearalenone and trichothecenes were produced by *Fusarium oxysporum* and *Fusarium solani* at 25-28 °C and pH5. When growing *Fusarium oxysporum* on different carbon sources. The amounts of zearalenone were in the order of xylose > sucrose > glucose > maltose > lactose > mannose. While, trichothecene amounts were in the order of glucose > maltose > sucrose > xylose > lactose > mannose. In case *F. solani* the efficiency for toxin production differs from *F. oxysporum* using the same carbon sources. Ammonium phosphate gave high levels of zearalenone and trichothecene (24.73 and 92.35 µg/ml). In case of *F. solani*, zearalenone was high in presence of casein (319 µg/ml). On the other hand, ammonium molybdate gave a high concentration of trichothecene.

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MUTAGENIC POTENTIAL OF AFLATOXIN PRODUCED BY ASPERGILLUS PARASITICUS AND ITS EFFECT ON GROWTH AND YIELD OF VICIA FABA.

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In this investigation the mutagenic potential of different seed soaking treatments with the toxin was evaluated by studies on mitotic division and chromosomes in *Vicia faba* root tip cells. It is also examined by observing the action of the applied treatment on DNA and RNA as well as on the electrophoretic pattern of seed proteins. In addition, the effect of the used toxin on germination, root and shoot growth, biomass and yield was investigated. The total aflatoxin (B₁, B₂, G₁ and G₂) produced by *A. parasiticus* induced a significant reduction in mitotic activity that is associated with a reduction in the amount of DNA and RNA. The toxin also induced several chromosomal abnormalities, the most common types are stickiness, disturbance, diagonal mitotic phases, chromosomal bridges, breakage and the formation of micronuclei in interphase cells. The applied toxin also induced variation in band number and intensity in the electrophoretic seed protein profile, which may indicate the over or under expression of some polypeptides and the synthesis of novel polypeptides under the effect of this toxin. The used treatments of *A. Parasiticus* total toxin resulted in reduction of germination, root, and shoot growth and biomass productivity. This toxin also caused reduction in a number of yield parameters including number of flowers, pods and seeds, per plant and the average weight of one seed.

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EFFECTS OF KHAT ON THE THYROID GLAND OF ALBINO RAT.

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Khat extract 0.2, 0.4 and 0.8 ml respectively, was given to three groups of albino rats. in addition to a control group. The thyroid glands of these animals were examined as well as stimulation of T3& T4 in their blood. Histologically, the 0.2 ml group showed marked activity as evidenced by smaller follicular size, low columnar principal cells with vacuolated cytoplasm, scalloped colloid and intense reaction to PAS stain. These changes were present in the 0.4 ml group, but to a less extent. The 0.8 ml group showed signs of underactivity. T3 & T4 levels were nearly doubled in the 0.2 ml group, but in the other two groups, they were not statistically different from the control. The causative factors are not known, but a direct effect on the thyroid, central effect on the hypothalamic- pituitary axis, or indirect effect through liver derangement, are proposed.

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EFFECTS OF KHAT EXTRACT ON THE OVARIES, PITUITARIES AND SUPRARENTAL GLANDS OF ALBINO RATS.

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Twenty Albino rats, assigned into 4 groups, were injected intraperitoneally with 0.2, 0.4, 0.8 and 2.0 ml of Khat extract. A fifth group of 4 animals was used as control. All animals of the group subjected to the highest dose i.e. 2 ml died within 24 hours. This could be ascribed to suprarenal failure, especially of the zona glomerulosa, concerned with mineralocorticoids secretion. Oocyte degeneration was observed with the lowest dose (0.2 ml) and it is attributed to a direct effect of Khat on oocytes, possibly chromosomal doubling. The doses (0.4 & 0.8 ml) resulted in basophilic hyperplasia of the pituitary together with stromal hyperplasia of the ovary and increased oestrogen production, while the corpora lutea, so formed, were haemorrhagic and secreted less progesterone. The neurohypophysis exhibited newly formed cells, which are suggested to be a phagocytic reaction to cathinone which crosses the blood brain barrier.

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CYTOGENETIC EFFECTS OF KHAT EXTRACT IN ALBINO RATS.

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Extract of Khat (50g *Khata edulis*, Forsk), was injected in 24 male and female rats divided into control, 0.2ml, 0.4ml, and 0.8ml dose-groups with a fifth group receiving 2 ml/ day (10 times the calculated dose). The last group died within 24 hours. The cytogenetic effects in these animal - groups were studied by examination of bone marrow of sacrificed animals, Structural aberrations increased significantly in the treated groups as compared to the control one. In the treatment groups, these changes appeared in the 0.2 ml dose group and increased significantly as the dose increased to 0.4 ml, quadrupling the dose increased the incidence of these changes but insignificantly. Also numerical aberrations showed a comparable difference. A mutagenic effect of Khat is inferred.

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NICOTINIC RECEPTOR INVOLVEMENT IN THE NEUROTOXICITY OF A PYRETHROID PESTICIDE 'CYPERMETHRIN' IN MICE.

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Cypermethrin is a pyrethroid pesticide that belongs to class II. It produces neurotoxicological responses as a result of increased Sodium influx into the axons leading to unstable nerves. This leads to a variety of symptoms, controlled presently by symptomatic management and a search for suitable antidote is going on. It has been reported that nicotinic antagonists aggravate pyrethroid toxicity. The present study investigates the protective effect of nicotine (0.1 mg/Kg I.P.) on the neurotoxic manifestations of cypermethrin at 1/6th LD in mice. Interaction with atropine (10 mg/Kg I.P.)⁵⁰ has also been studied and the probable involvement of nicotinic receptors in manifestations of neurotoxicity will be discussed.

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PROBABLE ROLE OF NEUROTRANSMITTERS IN THE MANIFESTATIONS OF NEUROTOXICITY BY PESTICIDES.

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The present study investigates interactions of pesticides with various CNS drugs and the probable mechanisms involved. The experiments were done in mice at one-fourth LD₅₀ of pesticides viz. Aldrin (organochlorine), Phosphamidon (organophosphorite), Chlorpromazine, Diazepam, Leptazol and Tremorine. It was observed that the drug effects were significantly enhanced after acute pesticide exposure and were markedly decreased after subacute treatment for 8 weeks with one-fortieth LD₅₀. Various neurotransmitter blockers such as Atropine, Alpha-methyl-p-tyrosine, p-chlorophenyl-alanine etc. were used to elucidate the probable mechanism involved. Such interactions may provide an additional variable factor affecting therapeutic efficacy of drugs in developing countries, where the population at large is exposed to high residual concentrations of various pesticides. The significance of the results shall be discussed.

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TOXIC AND GENOTOXIC EFFECTS OF METHYL BROMIDE IN WHEAT AND BARLEY GRAINS.

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Methyl bromide (MeBr) is used for grain protection in storage. The present investigations aimed at studying the toxic and cytogenetic effects of MeBr in wheat and barley grains. Grains of *Triticum aestivum* and *Hordeum vulgare* were fumigated with the doses 25 and 50 g / m³ for 4 hrs. X 1, 2, 3 and 4 days and stored for one, two and four weeks. The long periods of fumigation with MeBr inhibited grain germination and affected root and shoot growth of both plants. Fumigation of wheat and barley grains inhibited cell division and caused a high percentage of abnormal mitoses. The dominant types of chromosome abnormalities were: chromosome stickiness, disturbed meta- and anaphases, faint and non-stained chromosomes. Fumigation of the grains with 50 g/m³ MeBr for the longest period had nearly no effect on meiosis. The present studies revealed that *Triticum aestivum* grains are more sensitive to MeBr than *Hordeum vulgare* grain. Fumigation of the grains with 25 g/m³ MeBr for 4hr. X 4 days inhibited grain germination and cell division and induced statistically significant percentage of abnormal mitoses even after storage of the grains for one week. The percentage of seedling emergence was 24.5% only.

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CYTOGENETIC EFFECT OF THE HERBICIDE "DICAMBA" IN SOMATIC AND GERM CELLS IN MOUSE.

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The cytogenetic effect of the herbicide "Dicamba" was investigated in mouse spleen, bone marrow and testis. Swiss mice were intraperitoneally injected with 20 mg/Kg body wt. "Dicamba" (1/10 LD₅₀) then killed 6, 24 and 48 hr. after injection. In another experiment mice were orally treated by gavage. Single and multiple treatments for 3 and 5 days were conducted with the dose 119 mg/Kg body wt. (1/10LD₅₀) and mice were sacrificed 24hr after the last treatment. The percentage of chromosome aberrations was high after exclusion of the number of metaphases with gaps. The effect of "Dicamba" was maximal 6hr after intraperitoneal injection in both somatic and germ cells. Oral treatment by gavage induced also a high percentage of chromosome aberrations in mouse bone marrow, spleen and germ cells. This percentage was statistically significant and increased by increasing the number of treatments with the herbicide. The dominant chromosome aberrations were gaps, fragments, chromatid deletions in somatic cells and autosomal, x-y univalents and polyploidy in germ cells. The present results indicate that "Dicamba" is genotoxic in : more bone marrow, mouse spleen and mouse testis.

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GENOTOXIC ACTIVITY OF CARBOPLATIN ON CULTURED MAMMALIAN CELLS.

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Carboplatin, an antitumor drug, was evaluated on murine erythroleukemic cells (GM-86) and Chinese Hamster ovary cells (CHO) for its genotoxic effects. Drug concentrations ranging from 1 to 10 micrograms per ml. were used continuously for 24, 48, and 72 hours. Cell multiplication and Viability were affected noticeably in both cell lines, but more so in GM-86 cells. The treatment also resulted in a concentration dependent decrease in DNA synthesis in GM-86 cells determined through both the scintillation counter and autoradiography techniques. Carboplatin significantly, increased the frequency of chromosomal aberrations and micronuclei formation in GM-86 cells. An inhibitory effect on the mitotic index of GM-86 cells was also observed with increasing dosage and durations of carboplatin exposure. CHO cells treated with the same concentrations of the drug produced noticeable but comparatively lower frequency of chromosomal damage and micronucleation. The results suggest that carboplatin's genotoxic effects are more pronounced in the malignant GM-86 cells, indicating the drug's preferential genotoxicity to cancerous cells.

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MORPHOLOGICAL AND GENOTOXIC EFFECTS INDUCED BY ANABAENA FLOS- AQUAE EXOTIN IN VICIA FABA.

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Many species of blue green algae (Cyanophyte) produce which cause great problems to plants, animals and man. The present study was done to illustrate the effect of *Anabaena flos- aquae* (toxic species) on both mitotic division, growth and product of *Vicia faba* plants. The seeds of plants were soaked on supernatant of well grown *Anabaena flos- aquae* culture for different hours (2, 4, 6, 12 and 24 hours) and then planted. The cytological studies included mitotic index, total percentage of abnormalities and percentage of each type of abnormalities. The cytological studied included mitotic index, total percentage of abnormalities and percentage of each type of abnormalities. The algal toxin caused a highly significant reduction in the mitotic index in *Vicia faba* root tips and induced a high percentage of abnormalities. All treatments caused a decrease of R, No. of secondary roots, size of seeds perpod, leaves per plant and also decreased the number and size of nodules. The value of nutrient concentration in *Vicia faba* tissues was decreased for within 2-24 hrs.

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CYTOGENETIC ACTIVITIES OF SOME HERBICIDES IN ALLIUM SATIVUM.

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The present investigation was carried out to examine the mitodepressive and chramotoxic effect of four herbicides, Tackle, Treflan, Stomp and Cobex. Their acton on DNA, RNA and protein contents in the roots of *Allium satiyum* was also studied. Results showed that the four herbicides, had a significant mitodepressive effect, even after recovery of the roots for 24 hours. Also they affected the mitotic phases and produced a number of chromosal aberrations. The most frequent abnormalities observed are spindle disturbance, stickiness , bridges, laggards and multipolarity. Moreover, the four herbicides affected the DNA, RNA and protein contents, where a depression in their values was noted.

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EVALUATION OF THE GENOTOXICITY OF SOME COMMON CHEMICALS USED IN ORDNANCE INDUSTRY WITH THE SOS CHROMOTEST.

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The SOS chromotest is a quantitative bacterial colorimetric assay for genotoxins as presented by Quillardet et al in 1982. It is based on the SOS response induced by DNA- damaging agents and realized by measuring the expression level of *sj iA* gene in *Escherichia coli* PQ35, PQ37. It is also the rapidest and simplest method to detect genotoxicity in liquid quantitatively. In our tests, the genotoxicity of three kinds of explosives, trinitrotoluene (TNT), hexogen (RDX), and nitroglycerine (NG) was detected with this method as a standard procedure. The tester strains PQ35 and PQ37, kindly supplied by Dr. M. Hofnung, were incubated at 37°C with shaking. The Three chemicals tested were dissolved in dimethyl sulfoxide (DMSO) and diluted to 0.001, 0.01, 0.1, 1, 10, 100, 1000 µg / assay. As a positive control, benzo [a] pyrene (B[a]P) was used in experiments with metabolic activation (S9 mix) and mitomycin C (MMC) was used in experiments without metabolic activation, while normal saline and DMSO were used as the negative controls. Two hours after chemicals addition into the incubated tubes, the activation of β- galactosidase and alkaline phosphatase in PQ35 and PQ37 with or without s9 mix were measured. The ratio R and the induction factor I were calculated as the formulae of the standard procedure. The positive response was judged when I reached 1.5 or more. Results showed that MMC (S9-), B (a)P(S9-) in both PQ35 and PQ37 induced evident SOS response and the induction factor I was up to 10.2 and 2.6 in PQ35. 6.0 and 3.9 in PQ37, respectively, accompanied by typical dose- response curves, showing that both are SOS inducers. The tested chemical, TNT in both tester strains with or without S9, RDX in PQ 37 and NG in PQ35 without S9 gave positive responses while RDX and NG in both strains with S9 and RDX in PQ35, NG in PQ37 without S9 gave negative responses. These results show that TNT is an SOS inducer while RDX and NG have some SOS induction. It indicates that the three chemicals tested may have DNA- lesions and potential genotoxicity.

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GENOTOXICITY OF THE CARBAMATE INSECTICIDE "SEVIN" IN MOUSE BONE-MARROW.

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The carbamate insecticide "Sevin" possesses broad insecticidal activity. The ability of "Sevin" to induce micronuclei, chromosomal aberrations and sister chromatid exchanges in mouse bone-marrow was investigated in order to evaluate its potential mutagenecity. Single and double intraperitoneal injection of mice with the dose 12 mg

"Sevin" Kg^{-1} body wt. induced a significant increase in the percentage of micronucleated polychromatic erythrocytes (1.4) compared with 2.7 after i.p. treatment with 1 mg / Kg. body wt. "Mitomycin C" (positive control). The same dose caused marrow toxicity after double injection as indicated by a significant increase in the percentage of polychromatic erythrocytes (PEs). Dermal treatment with the dose 500 mg Sevin / Kg body wt. induced a statistically significant increase in the percentage of micronucleated PEs (1.7). The dose 35 mg "Sevin" Kg^{-1} body wt. induced a statistically significant increase in the percentage of chromosomal aberrations 6, 24 and 48 hr. after i.p. treatment. Such percentage decreased linearly as the time after the treatment increased. The percentage of chromosome aberrations reached 14.9 ± 0.39 48 hr. after treatment compared with 16.7 ± 0.40 48hr. after i.p injection with 1 mg Kg^{-1} body wt. "Mitomycin C". Sevin induced mainly structural chromosomal aberrations. The most common types of aberrations, which appeared included deletions, gaps and fragments. "Sevin induced a dose dependent increase in the frequency of SCE's in mouse bone marrow cells. The doses tested were (3.5, 9, 18, and 35)mg Kg^{-1} body wt. The maximum value reached (10.1 ± 0.39)%. The present results indicate that "Sevin" is genotoxic in mouse bone- marrow . Accordingly much more care should be taken in using "Sevin" in agricultural crops.

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EFFECT OF MERCURY ON BONE MARROW CELL DIFFERENTIATION

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The effect of mercuric chloride (HgCl_2) on differentiation of bone marrow cells into granulocyte / macrophage lineage cells was investigated. Bone marrow cells were isolated from 6-8 week old Balb/ c mice, mixed with appropriate concentrations of HgCl_2 (final concentration : 0.01- 5 μM) and cultured *in vitro* for 6 days under the influence of granulocyte- macrophage colony stimulating factor (GM- CSF). The results showed that *in vitro* exposure to mercury does not have any direct effect on the differentiation of bone marrow cells in spite of decreased cells viability. To examine whether there is any difference between *in vitro* and *in vivo* treatment of HgCl_2 , mice were treated with various doses (0.5, 2 mg/ kg) of HgCl_2 for 2 weeks intraperitoneally and bone marrow cell cultures were conducted. In contrast to the results from the *in vivo* exposure, *in vivo* HgCl_2 exposure significantly increased bone marrow cell differentiation (control : 21 ± 4 colonies, 0.5 mg/ kg : 34 ± 7 colonies, $P < 0.05$; 2 mg/kg : 54 ± 10 colonies, $P < 0.01$). In addition, *in vivo* HgCl_2 treatment significantly increased the relative weight of spleens. These data demonstrated that although mercuric chloride does not have any direct effect on bone marrow cell differentiation, *in vivo* exposure to mercuric chloride significantly increased bone marrow cell differentiation probably via indirect mechanisms.

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ANTIMUTAGENIC EFFECTS OF RUBROFUSARIN EXTRACTS OF CASSIA TORA SEMEN IN CHROMOSOME ABERRATION TEST.

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The roasted seeds of Cassia tora had been widely used as a Korean's favorite tea. In order to investigate the antimutagenic effect of Rubrofusarin which is a component of methanol extracts of Cassia Tora semen and already known to have an antioxidant effect *in vitro* system, *in vivo* and *in vitro* chromosome aberration tests were used for evaluating method. As a chemical mutagen, mitomycin C (MMC) and bleomycin have been chosen for their well-known mechanism of mutagenesis. β -carotene which has an antioxidant effect and now in phase III clinical trial as a chemopreventive agent by FDA was used as an index compound. Rubrofusarin lowered around 50% of bleomycin (4 μ g / ml) induced chromosome aberrations at the dose of 250 μ g/ ml *in vitro*. Within this experiment, β -carotene showed 50% inhibition of MMC induced chromosome aberrations. The antimutagenic effect of rubrofusarin *in vivo* chromosome aberration test using bone marrow cells of ddY mice medicated through po two hours before mutagen treatment showed much higher than the *in vitro* inhibitory effects against both MMC and bleomycin. All above results, rubrofusarin will be a candidate of chemopreventive agents.

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IMMUNOTOXIC EFFECTS OF INDOOR FORMALDEHYDE POLLUTION ON HUMAN HEALTH.

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Blood samples were collected from 61 residents and 127 furniture factory workers who were exposed to indoor formaldehyde. These samples were prepared to analyze immunological parameters. Immunoglobulins G, M, A and complement C3 were measured by using single radial immunodiffusion technique. T-lymphocytes and total lymphocytes were determined by ANAE method. Air samples were collected with passive sampler and formaldehyde was analyzed with MBTH spectrophotometer. The residents did not show significant changes on immune functions. However, the level of IgG in one group of workers, who was exposed to indoor formaldehyde at 0.341 mg/m³, decreased significantly when compared with the other workers.

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EFFECT OF PESTICIDES ON NEUTROPHIL FUNCTIONS IN SHEEP.

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Neutrophils are important phagocytic cells in peripheral blood of all living organisms. These are first line of defence against any foreign invasion. Reduction in number or functional activity of these cells may lead to decreased resistance to infections and occurrence of epidemics. To evaluate the effect of four commonly used insecticides on blood neutrophils; 20 lambs of 6 months age were taken and randomly divided into five groups of four lambs each. One group was kept as control and four groups were given orally lindane (1.25 ppm), monocrotophos (0.025 ppm), carbofurex (2.5 ppm), and fenvalerate (1.25 ppm) daily for six months. To measure the metabolic activity of the phagocytic cells, the nitroblue tetrazolium (NBT) reduction test was performed on peripheral blood neutrophils at monthly intervals. There was significant suppression of neutrophil functions as indicated by reduction by number of NBT positive cells in insecticides treated group in comparison to controls.

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IMMUNOTOXIC EFFECT OF LINDANE IN SHEEP: ASSESSMENT OF CELL MEDIATED IMMUNE RESPONSE.

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Increased pesticide use has resulted in environmental contamination and their residues appear in most food stuffs. The continuous intake of low levels of pesticides by man and animals may lead to various deleterious effects in body. To assess the effect of lindane on cell mediated immune response in sheep, 8 six months old lambs were taken and randomly divided in two groups of 4 lambs each. These lambs were vaccinated with *Brucella melitensis* rev 1 at day zero and day 90. One group was given lindane daily orally at dose rate of 1.25 mg/Kg body wt for 6 months. The lymphocyte stimulation test, total leucocytic count and absolute lymphocyte count were performed from blood collected at 10 days interval. Delayed type hypersensitivity (D.T.H) reaction was assessed at 6 months of observation. A highly significant suppression in total leucocytic count, absolute lymphocyte count, lymphocyte stimulation test and DTH reaction was observed in lindane fed lambs as compared to controls, which indicate the suppression of cell mediated immune response in sheep fed 1 lindane at no adverse effect doses.

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EFFECT OF NITRITE ON MUTAGENICITY AND IN VITRO PROTEIN DIGESTIBILITY OF SPIRULINA, SPP.

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Fresh, sun- dried and spray- dried of *Spirulina spp.* (THS-02, THS-04 and THS-10) were separately homogenized with dimethylsulfoxide (DMSO) ; then, they were incubated with nitrite in gastric simulated condition (pH 3.0, -3.5, 37°C, 4hr). The treated samples were determined for their mutagenicity using the Ames test and for nitroso compounds (expressed as nitrosomorpholine equivalent, NME). Ethanol extracts of *Spirulina spp.* with and without nitrite were tested for their effects on in vitro multienzyme digestion of bovine serum albumin. The results showed that DMSO extracts of *Spirulina spp.* were not mutagenic to strains TA98 and TA100. Interestingly, all soluble fractions of nitrosated products showed mutagenic potential to both tested strains. NME was also detected in soluble and insoluble fraction at the levels of 70-1,180 ng- mole/g of original weight and 480- 8,940 ng-mole /g of original weight, respectively. However, there was no correlation between the mutagenicity and content of NME in each sample. It was indicated that the extracts of nitrite treated *Spirulina spp.* contained non - nitroso mutagenic compounds. Moreover, ethanol extracts of spray - dried THS - 02, THS - 04, THS - 10, sundried THS - 02 and THS - 04 decreased the digestion of BSA . On the other hand, fresh sample of all strains as well as sun - dried THS - 10 and all nitrite treated samples except those of sun - dried THS - 02 and of spray - dried THS - 10 demonstrated their enhancing ability on the digestion of BSA. It was concluded that *Spirulina spp.* treated with acidic nitrite posted mutagenic potential but also as an inducer of protein digestion.

P 86

IMMUNOSUPPRESSION FOLLOWING K-OTHRINE AND SELECRON EXPOSURE IN MICE.

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The effects of K- Othrine and selecron on the immune function were investigated in weanling female mice receiving 1/10th LD50 of each insecticide in the diet for 8 weeks. The humoral immune response was measured by the antibody response against sheep red blood cells (SRBC), a T - cell - dependent antigen, and against *E. coli* endotoxin (lipopolysaccharide; LPS), a T - cell - independent antigen. Cell mediated immune response was evaluated by the delayed hypersensitivity reaction to keyhole limpet haemocyanin (KLH). Both insecticides suppressed the serum haemolysin titers and the direct (IgM) plaque forming cell (PFC) response against SRBC and the serum haemagglutinating titers to *E. coli* LPS. In addition, inhibition of the delayed hypersensitivity reaction was observed. Memory function was only affected by K-

othrine. Leukopenia and lymphocytopenia were produced by the 2 insecticides in addition to reduced cellularity of thymus, spleen and bone marrow (K-othrine) or bone marrow alone (selecron). It was concluded that both insecticides suppress the humoral and cell-mediated immune responses in mice.

P 87

IMMUNOTOXIC EFFECT OF CYPERMETHRIN ON HUMORAL IMMUNE RESPONSE IN CHICKENS.

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Pesticides are major contaminants of our environment and persist in various food stuffs including cereals, grains, eggs, meat and milk. The continuous intake of low levels of pesticides in body may cause altered immune response leading to vaccinal failure, increased susceptibility to various infections and allergic reactions. To study the effect of cypermethrin on humoral immune response in chickens 125 day old broiler chickens were procured and divided into 3 groups of 40 each. Five birds were utilized for 0 week observations. Birds of group I, were kept unvaccinated while group II and III birds were vaccinated with New Castle disease vaccine at day 4 and day 32. Group I and II birds were given normal broiler ration and served as unvaccinated and vaccinated controls, respectively while group III birds were fed 100 ppm cypermethrin in feed for 8 weeks. Serum globulins and gammaglobulins were estimated at weekly interval using blood of 5 birds from each group. Specific New Castle disease vaccine induced humoral immune response that was measured by HI and ELISA at weekly intervals. There was significant suppression in serum globulins, gammaglobulins and specific HI and ELISA antibodies in cypermethrin fed chickens in comparison to controls indicating immuno-suppressive effect of the pesticide.

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IMMUNOTOXIC EFFECT OF CYPERMETHRIN ON CELL MEDIATED IMMUNE RESPONSE IN CHICKENS.

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Environmental pollutants, such as pesticides, are widely distributed throughout the world. Continuous low level exposure to such chemicals may cause altered immune responses in animals, birds and man. To study the effect of cypermethrin on cell-mediated immune response in chickens, 125 day old broiler chicks were taken and divided into three groups of 40 each. Five birds were used for 0 week observations. The group I birds were kept as unvaccinated control, group II birds were vaccinated at day 4 and 32 and both groups were given normal broiler ration. The group III birds were vaccinated and fed a dose of cypermethrin (100 ppm in feed) for 8 weeks. The

lymphocyte stimulation test, total leukocyte count and absolute lymphocyte count were performed at weekly interval using blood of 5 birds from each group. Delayed type hypersensitivity reaction was monitored at 4th and 8th week of observation. A significant suppression in total leucocytic count, absolute lymphocyte count, lymphocyte stimulation test and delayed type hypersensitivity reaction were observed in cypermethrin fed birds as compared to controls, which indicate the suppression of CMI response in chickens fed cypermethrin at low doses.

Miscellaneous

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PATULIN PRODUCTION BY FUNGI ISOLATED FROM BARLEY LOCALLY GROWN IN SAUDI ARABIA.

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Patulin is a fungal toxin that can occur in contaminated feeds, particularly barley. The influence of seventeen fungal isolates from barley produced in Saudi Arabia, to produce patulin was tested *in vitro* using three different media i.e., barley (BM), potato dextrose agar (PDA) and yeast - extract sucrose (YES) broth. Patulin was produced by 70.6% of the tested isolates. The best medium for production of patulin by the fungi is PDA followed by BM, but none of the tested fungi grown on YES has yielded patulin. In BM, the quantities of patulin produced varied from 948 ug/kg barley produced by *Eurotium herbariorum* to 2448 ug/kg barley produced by *Aspergillus parasiticus*. The biological studies undertaken using chick embryos and *Bacillus subtilis* have confirmed the toxicity of the barley medium extracts.

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INSECTICIDAL ACTIVITIES OF TWO NEW COMPOUNDS FROM *ANNONA SQUAMOSA* LINN. AGAINST FOUR DIFFERENT PESTS.

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Two new compounds were isolated from the seed oil fractions of *Annona squamosa* Linn. These two compounds are annonastin and squamozin which were found to be toxic against four important crop pests such as *plutella xylostella* Linn., *Spodoptera littoralis* Bio., *Nilaparvata lugens* (stal) and *Drosophila melanogaster* Meig. Annonastin was found to be more toxic than squamozin; causing 50% mortality to the above mentioned pests at concentrations of 0.53, 0.57, 0.50, 0.55 and 0.80, 0.87, 0.80, 0.84 µg/ cm², respectively. The present study revealed that the newly isolated compounds could be used for the control of the above mentioned insect pests.

P 91

SYNTHESIS AND ANTIMICROBIAL EVALUATION OF SOME ACRIDINE DERIVATIVES.

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6,9- dichloro- 2- methoxyacridine reacted with P-aminoacetophenone to give the corresponding anilide derivative 2. The latter was converted to the chalcone analogues 3a-e, by reaction with different aldehydes. Condensation of the chalcones with hydrazine hydrate afforded 6-chloro-2-methoxy-9-[p-(5-aryl-2-pyrazolin-3-yl) anilino] acridine (4a-c). Similarly prepared, 6-chloro-2-methoxy-9-[p-(5-aryl-2-isoxazolin-3-yl) anilino] acridine (5a,b), as well as 6-chloro-2-methoxy-9-[p-(5-aryl-2-pyrimidin-3-yl) anilino] acridine (6a, b), upon reaction of the chalcones with hydroxylamine and /or urea respectively. Antimicrobial screening of the prepared compounds was performed against 6 microorganisms which showed moderate to high activities for some of them.

P 92

WATER QUALITY IN SOME OF THE OLD AIN ZARKA UNDERGROUND WELLS IN ALMADINAH ALMUNWARRAH.

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The water quality in nine underground water wells in old Ain Zarka, Almadinah Almunwarrah, Saudi Arabia, in five years span is investigated. Parameters such as pH, [Cl⁻], [SO₄²⁻][NO₃⁻], [Ca²⁺] as well as the total dissolved solids (T.D.S.) are reported and are explained in terms of their yearly variation and water quality standards.

P 93

PROTON INDUCED X- RAY FLUORESCENCE ANALYSIS OF LEAD IN THE AIR OF ALMADINAH ALMUNWARRAH.

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Lead in the air of several locations in Al - Madinah Al- Munwarrah, Saudi Arabia, has been measured using the proton induced X - ray fluorescence method (PIXE). A comparison is made with average lead concentration in Jeddah. It is found that lead concentration in the air of Al- Madinah Al- Mounawarrah is much less than that in Jeddah.

P 94

EXCHANGE OF Zn, V, Cd AND Hg USING ZEOLITE A AND DINONYLNAPHTHALENE-SULPHONATE.

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Zeolite Na A and sodium dinonylnapthalene-sulphonate (Na DNNS) have been used to decontaminate and recycle Zn, V, Cd and Hg ions from a textile fabric waste waters. A comparative study of the kinetics, temperature, ionic strength and pH effects of the uptake of the mentioned cations by the two exchangers is made. It is concluded that NaDNNS has certain advantages over zeolite NaA.

P 95

INFLUENCE OF PROTEIN MALNUTRITION ON TERATOGENICITY AND EMBRYOTOXICITY OF SOME ANTIEPILEPTIC DRUGS IN RATS.

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Protein malnutrition (PM) has been found to enhance incidence of embryotoxicity of some drugs, an affect which should be carefully assessed especially in case of drugs of low therapeutic margin or those need to be used for long duration of time. The present work aims at evaluating the possible effects of PM on teratogenicity and embryotoxicity of two drugs commonly used in antiepileptic therapy, namely Diphenylhydantoin (DPH) and phenobarbitone (PB). The studies were conducted on Sprague- Dawely rats. Animals were either normally fed or protein- malnourished receiving standard diet of 20% or 5% casein, respectively. Each drug was applied in oral daily doses during days 7 to 15 of gestation (sperm appearance = day 1). Doses of DPH were 250, 500, 750, 1000 mg/Kg. Those of PB were 25, 50, 75, 100 mg / Kg. In addition, influence of PM on interaction between DPH (500 mg/Kg) and PB (50 mg/ Kg) has been also evaluated. The results obtained indicated that protein malnutrition potentiated the embryotoxic and teratogenic responses to DPH and PB as evident from the found changes in growth parameters, external, internal and skeletal malformations.

P 96

SUBACUTE TOXICOLOGICAL STUDY ON INHALATIONAL EXPOSURE TO MOSQUITO KILLER INSECTICIDES IN RATS.

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The present work aims at evaluating the possible subacute toxic consequences following exposure to mosquito killers. Two brands have been investigated. Brand I (Hesh) contains bioallethrin alone, while brand II (Killing) contains bioallethrin plus piperonyl butoxide. 130 adult Sprague- Dawley rats have been divided into 3 main groups. One group served as an untreated control, while the other two groups were daily exposed in a static system to a fixed dose of the insecticide (20 minutes) for 5 days. Five main types of evaluations were investigated : 1) haematological changes , 2)biochemical changes ; 3) gastric pH ; 4) gastric emptying time; and 5) bacterial challenge test 9 using *S.typhimurium*).The results obtained indicated that both evaluated brands did not induce any significant changes on any of the tested parameters except marked elevations in the eosinophils count and in the serum levels of GOT and alkaline phosphatase. In addition, the tested brands induced significant increase in gastric as well as significant decrease in the gastric emptying time.

P 97

FORMALDHYDE IN MILK ANALYTICAL AND TOXICOLOGICAL STUDIES.

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Fifty samples of both fresh and preserved milk were collected from different localities (Tanta, Alexandria and Cairo governorates). These were analysed for the presence or absence of formaldehyde. Mean formaldehyde concentration in these samples was used as a guide in calculating the dose for the experimental animals. The experimental study was carried out on 24 male Albino rats that were divided into 3 groups, one control group, and 2 experimental groups, (acute and chronic formaldehyde administration). Albino rats fed on formaldehyde containing milk samples showed liver, kidney and brain pathologic changes that were more evident in the chronically exposed animals.

P 98

EVALUATION OF PROGESTERONE PRETREATMENT ON CADMIUM-INDUCED TOXICITY IN MALE RATS

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Acute cadmium (Cd) toxicity was found to produce testicular, hepatic and renal damage. The testicular effects of Cd was found to be prevented by means of several specific treatment including progesterone. However, more recently it has been found that progesterone pretreatment increased the lethality of Cd but had no effect on

testicular toxicity. Therefore, this study was carried out to assess the effects of progesterone pretreatment on Cd toxicity in rats. Acute Cd toxicity was induced by a single s.c. injection of either 10 or 20 μmol . CdCl_2 / kg into male albino rats. Other groups of animals were pretreated with progesterone (100 mg/kg,s.c) for 3 consecutive days. Then CdCl_2 (10 or 20 μmol ./kg) was injected concomitantly with the last injection of progesterone. 24 hr later, animals were killed then different tissue metal contents as well as histopathological examination of different organs were carried out. Liver and Kindney functions were also assessed by measuring serum ALT, creatinine and BUN. The results and the effect of progesterone pretreatment on Cd induced toxicity in rats to be discussed.

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